Dry Powder Inhalation (DPI): the cornerstone of efficient inhaled drug delivery

What do physicians[1] think of DPIs?

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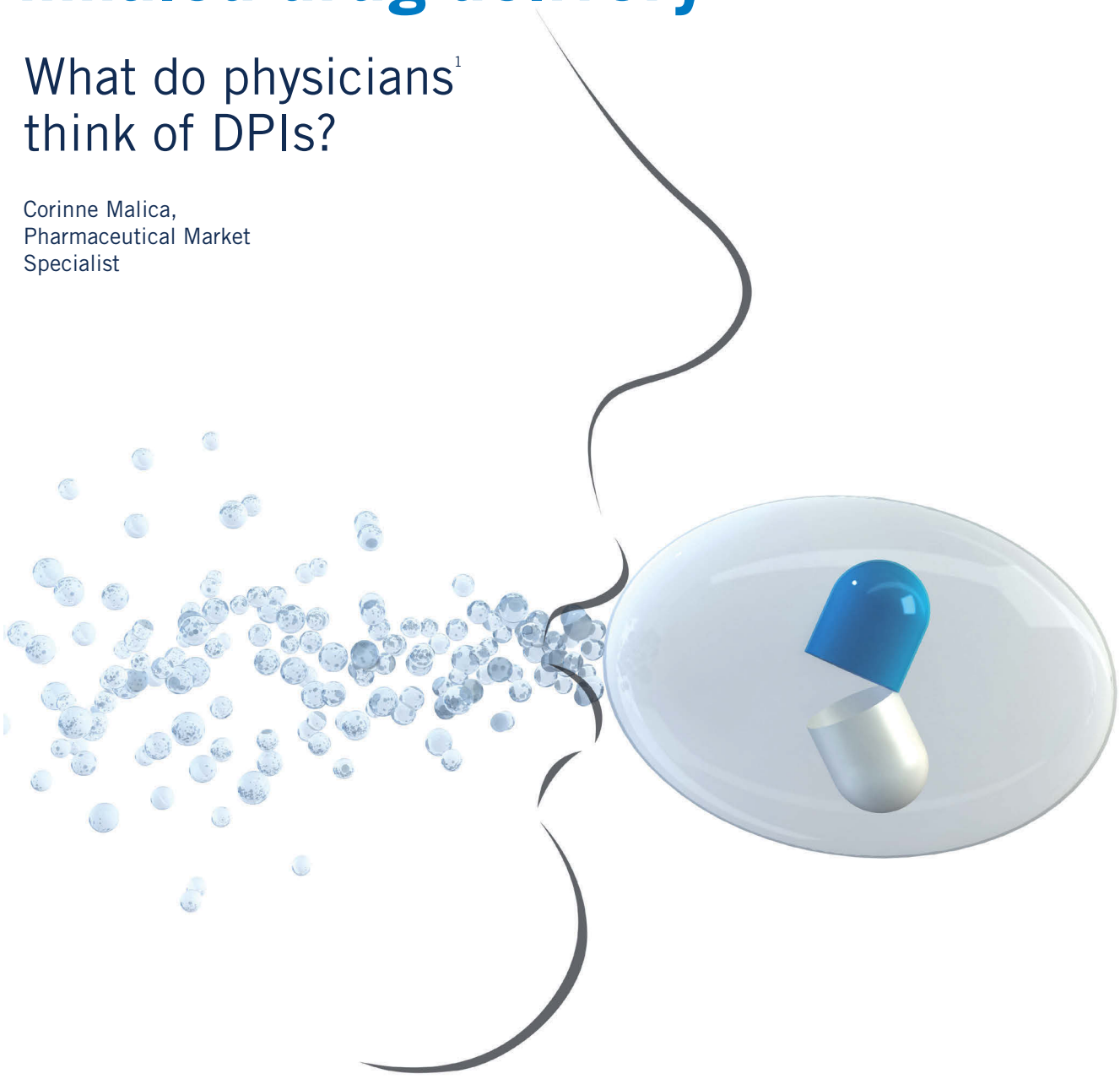
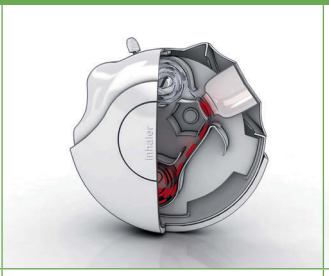


Introduction

Drug delivery to the lungs by the inhaled route is usually achieved with one of three device concepts – pressurised metered-dose inhaler (pMDI), dry powder inhaler (DPI), or nebuliser. Historically, the portable treatment of asthma and chronic obstructive pulmonary disease (COPD) has involved the use of drugs delivered mostly by pMDI. However, due to the need for press-and-inhale co-ordination for optimal drug delivery and issues surrounding propellants and environmental sustainability, these devices are not the top of mind choice for new treatment. Subsequently, interest in DPIs as an alternative to traditional pMDIs has burgeoned in recent years following advances in their design and performance.[2]

Currently marketed DPIs are all passive, breath-actuated devices, relying on the patient's inspiratory flow to disperse the powder formulation and deliver it to the lungs. A number of proprietary and generic devices have been developed with important differences in design and handling. From the clinicians' perspective, educating the patient in the correct use of an inhaler is critical to optimising patient compliance and thus ensuring effective treatment.[3] We sought the views of treating physicians in France (GPs and lung specialists) and Turkey (lung specialists) on four inhalation devices – three DPI devices (capsule-, blister- and reservoir-based) and the pMDI.

Capsule DPI	Blister DPI	Reservoir DPI	pMDI
			
• Encapsulated drug • Fixed dose	• Drug packaged in blister packs • Fixed dose	• Drug contained in storage reservoir • Metered dose transferred to dosing chamber prior to inhalation	• Pressurised canister containing active drug, propellants, surfactants, and preservatives • Doses released through a metering valve

Treatment success – mostly depends on the delivery system

In our survey, the primary consideration for treating physicians is the choice of molecule, adapted according to the severity of disease and prior treatment. For example, mild intermittent asthma would warrant a short-acting bronchodilator as relief treatment of acute attacks. If attacks were more moderate or persistent in nature, long-term treatment with a long-acting bronchodilator and/or inhaled steroid would usually be prescribed. Once the patient is stabilised on long-term treatment, a fixed combination product is generally preferred for maintenance therapy, with the possibility to adapt the dose as symptoms evolve.

However, non-compliant use of the delivery system was cited as the principal cause of treatment failure. When this occurs, physicians look to switch to another system if the prescribed molecule is available in other devices. When there is no option to deliver the same treatment with another system, physicians try to work with the patient to achieve correct use of the original device.

If, on the other hand, the delivery system has been correctly used and it is the molecule that is ineffective, physicians may opt to change or add to the treatment according to the evolution of the disease. In these cases, it is preferable to retain the delivery system if the new molecule is available with it, thereby avoiding a change of system.

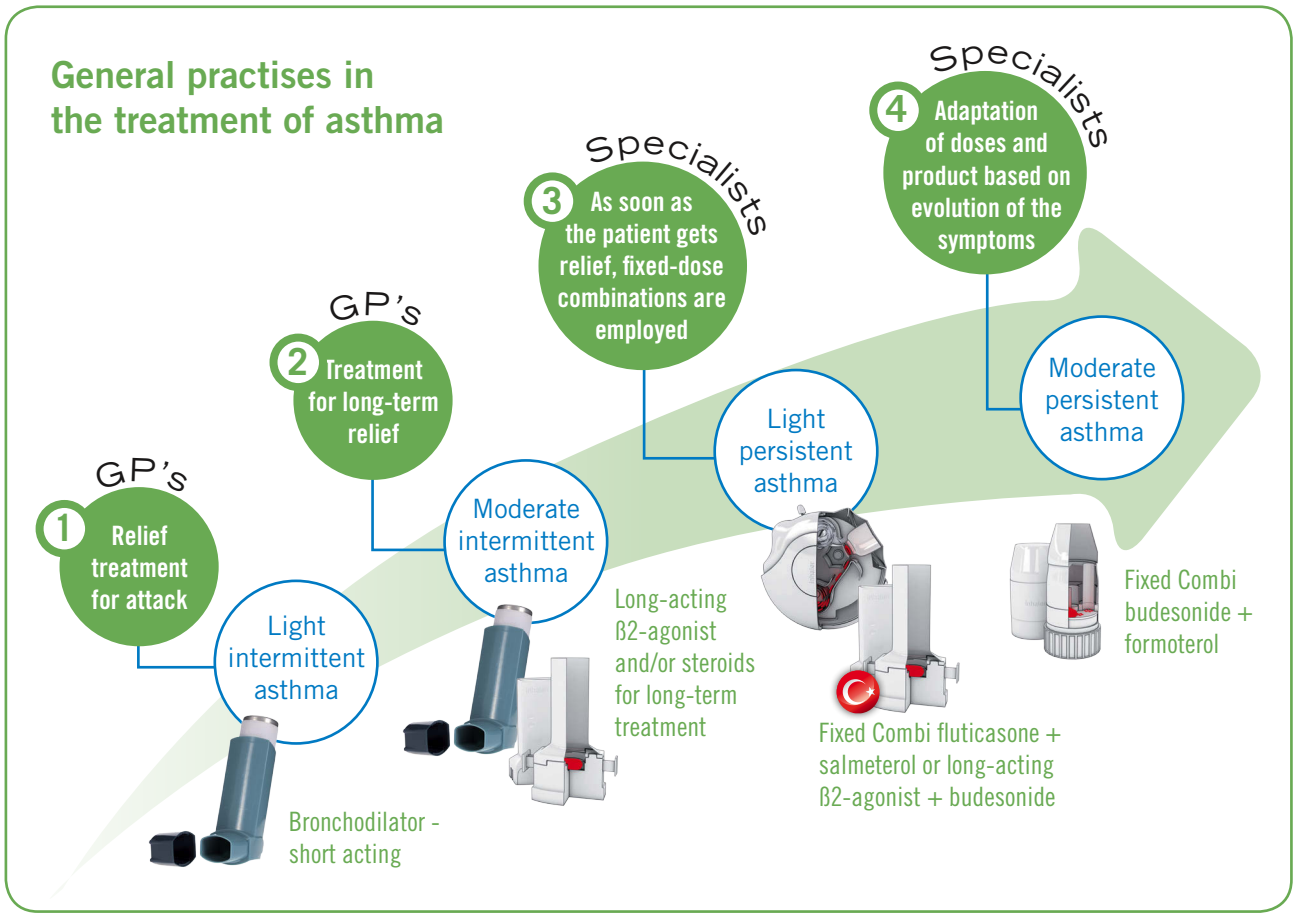
> *"Mainly, ineffectiveness of the treatment is due to non-compliant use of the system"* ***(Lung specialist, France)***

Choice of delivery system is therefore an important, secondary consideration, depending on the options available.

In Turkey, physicians are fortunate to have a broad range of products available that allows them to adapt both the device and the molecule to suit the patient. The patient's age, medical history (especially problems of co-ordination or dexterity), and lifestyle are taken into account. Turkish lung specialists may take between 10 to 15 minutes to explain and demonstrate the various

systems that are available to their patients to help with decision making.

In comparison, French physicians have a relatively restricted range of products to choose from and the choice of molecule usually dictates the device to be used.



Relations with the pharma industry – an opportunity to stimulate prescribing

Marked differences were evident between France and Turkey in the level of contact and the number of pharmaceutical companies active in the asthma field. In our sample, French doctors reported visits from only two multinational companies. In contrast, Turkish specialists had contact with many multinational and local companies, with close competition between key players.

> *"I receive leaflets but I don't give them out because it's complicated for patients and there's no more than there is in the instructions"*
> ***(Lung specialist, France)***

Turkish specialists also benefit from regular educational programmes and events, run by academic organisations such as the Turkish Thoracic Association and sponsored by pharmaceutical companies. These initiatives are a major source of information on the latest treatments and their use. In France, the physicians we interviewed were aware of only a few educational events being provided or sponsored by pharmaceutical companies.

Physicians in both France and Turkey receive leaflets for patients and sample devices for demonstration purposes from pharmaceutical companies. In general, the leaflets are considered of limited use because they focus on the product rather than the device and are not generally given out. In France, demonstration devices have only been available for pMDIs and two DPI inhalers (one blister-based and one reservoir-based).

Physician attitudes and awareness – affected by market maturity

Perhaps not surprisingly, the pMDI "spray" device was the most familiar device across the three groups surveyed. Physicians remembered capsule-based, blister-based, and reservoir-based DPI devices. A notable difference was familiarity with the capsule-based DPI device, which was greater in Turkey than France.

In France, products are generally not available in multiple delivery systems and subsequently there were some distinct associations with products and devices: pMDI "spray" associated with a specific acute relief treatment product; blister-based DPI and reservoir DPI each associated with a specific blockbuster product.

The situation in Turkey, with a much more mature asthma market, is rather different. Lung specialists have access to several options with regard to the combination of product and device, including generic products. Interestingly, attitudes to generic products revealed a general acceptance of generic devices, whereas generic molecules were more scrutinized.

Overall spontaneous awareness of devices

Spray

- Always remembered by all physicians in Turkey and France
- Quoted first in France and by many pneumologists in Turkey

Blister

- Quoted second generally by all physicians
- First DPI system quoted

Reservoir

- Quoted second like the Blister
- Always spontaneously associated with the top selling brand in reservoir-based system (Turkey & France)

Capsule

- Quoted in first position or after Blister in Turkey
- Always quoted in last position in France

The ideal inhaled drug delivery system – a consensus reached

Aside from the specific technological aspects of inhaled drug delivery – e.g. the physicochemical properties of the powder formulation, its fluidisation, dispersion and lung deposition – there are several design aspects to an inhaled drug delivery system that affect its practical use. These have implications for patient acceptance of, and compliance with, inhaled treatments.

During our survey, physicians identified four principal factors that for them define the ideal inhaled drug delivery system that would help to optimise patient use:

1. Ease of use/handling
2. Control of dose taking
3. Portability
4. Multi-dose system

In terms of handling, some patients may have limited strength, dexterity or co-ordination due to age or illness; others may have a limited ability to understand more complex usage instructions. It is therefore important that the device may be correctly used in a broad range of patients, including those with a certain degree of physical disability and those with limited cognitive skills.

Control of dose taking is an issue that is quite specific to inhaled drug delivery systems and is necessary to ensure efficacy. With DPIs, the dose must first be loaded correctly and any means to confirm this has been done is reassuring to the patient. Furthermore, the ability to feel that the product has been released is helpful, as is the case with several formulations that leave a slight taste in the mouth. Some form of dose counting is also particularly useful for the patient to make sure he/she is not left short of treatment.

Portability primarily means that the device should be easy to carry in all circumstances so that the patient may continually have ready access to treatment – especially important for the treatment of acute attacks. Devices should therefore not be too bulky. In addition, patients prefer a device that does not attract attention in order to avoid the stigma associated with diseases such as asthma.

Lastly, the system will ideally be able to deliver multiple doses in order to avoid too much handling, to reduce the number of components of the system, and to facilitate treatment while at school or work, while travelling, or while staying away from home.

Existing inhaler systems – room for improvement

In our survey, we focused on pMDI and capsule-based, blister-based, and reservoir-based DPI devices

pMDI

This well-known device is usually the first to be prescribed to a patient in the form of a product for fast relief from acute attacks; as a consequence, it is associated with a fast action and seen as a "saviour".

> *"If you teach the patient there are good results; the problem is that you cannot teach everybody"* ***(Lung specialist, Turkey)***

Physicians appreciate its simplicity above all – it's a multi-dose system that requires no loading and is small enough to fit into a pocket, making it easy to carry. It is also relatively inexpensive.

> *"People who use it too much shouldn't be given it. Some people use the one month refill in one week. Fear of overdosing and tachycardia"* ***(GP, France)***

However, the requirement for press-and-inhale co-ordination to achieve adequate delivery to the lungs is seen as a major drawback. In addition, the lack of a dose counter can be a problem if it leads to overuse of the medication if the patient is unsure they have received the dose correctly, or if the patient is unaware that they have run out of medication. The potential for abuse or addiction was also reported.

Blister-based DPI

The unique appearance of this eye-catching device makes it an attractive system for some; usually produced in vibrant colours, it is felt to be more suited to young people. However, its size is thought to make it too bulky to put in a pocket

> *"It is a device that deserves our confidence, patients like it, find it funny, it is very quickly adopted"* ***(Lung specialist, France)***

It is appreciated for being a multi-dose system that requires minimal handling, so for those who get on with it well it may prove to be fast to use and therefore useful for busy, working people. Others, however, may find it difficult to handle, with the lever in particular not well understood by some patients who often forget to re-arm it, or do so several times. In Turkey, the general consensus was that it is not suitable for the elderly or patients with limited abilities.

> *"Not very user-friendly, a bit small for some hands and too big for others, limited number of doses"* ***(GP, France)***

The presence of a dose counter may help prevent patients from running short, although the counter is too small to read for some patients and is not very precise in relation to confirming a dose has been taken. A further aspect that could be improved upon is the mouthpiece, which is felt to be too small to achieve correct inspiration. Cost may also be a barrier in some instances.

Reservoir-based DPI

In general, the reservoir-based DPI is considered a practical system, being a multi-dose device that fits easily into a pocket. The fact that it is offered with products for acute treatment as well as long-term treatment is a major advantage. Its mouthpiece is broad enough for easy inhalation and in Turkey the presence of a humidity sensor aids suitable storage.

> *"I prefer this device because of the fixed combination and multi-doses and the humidity sensor part but not happy from the patient's side because it is complicated to see the counter and if it is unreadable the patient returns it"* ***(Lung specialist, Turkey)***

A key fault is that with existing products there is no taste sensation to indicate that the dose has been taken correctly, and coupled with a somewhat small and imprecise dose counter (counts doses in 5s) patients may be left wondering if their asthma will be effectively controlled.

> *"Since they can't feel anything older patients don't like it but young people can do it"* ***(Lung specialist, Turkey)***

A further downside relates to the dose loading system, which may be difficult to understand for some patients and difficult to handle for others.

Overall, it was felt that this system is more suited to young, working people.

Capsule-based DPI

This system is valued for engaging the patient and making the taking of medication tangible – patients can see the capsule when loading and ejecting it, they can hear the capsule being pierced in the device, and they can taste the medication when they inhale; when the capsule is empty, they have additional confirmation that the dose has been taken. All these aspects provide reassurance to the patient that they are receiving their treatment correctly; furthermore, the evaluation of remaining doses is precise.

> *"For lower social class it is important to see the dose. This population is hard to convince"* ***(Lung specialist, Turkey)***

These benefits, however, come with the disadvantage that there is more handling required than with other devices. For unit-dose devices, the bulkiness of a separate system for the medication and device is another disadvantage.

> *"There is laborious preparation whereas with the others everything is set up, if you're only doing that once a day it's acceptable"* ***(GP, France)***

At a country level, this device is the most widely used device in Turkey across all patient types, whatever the age or social class. In France, by comparison, its use is limited by its restricted availability, being seen as a medication essentially for COPD and used mostly by specialists.

Capsule-based DPI systems – the preferred approach

We performed a final exercise by asking physicians to evaluate each of the four devices in comparison with each other.

In our groups, the capsule-based DPI system was the preferred system overall across all physicians and by physician (lung specialist and GP). There was also a high level of satisfaction with the blister-based DPI system in Turkey (among lung specialists), and the reservoir DPI system in France (among lung specialists and GPs).

In terms of system key attributes, the capsule-based DPI system was generally considered 'easy to use', 'fits well with physician expectations' and 'fits well with patient needs'. The blister-based DPI system was seen as 'powerful', 'appealing', and 'unique' and the reservoir DPI system as 'innovative'. Finally, pMDIs were highly cost acceptable.

Conclusions

There are many practical aspects to inhaled drug delivery systems that can have a significant impact on the likelihood of patient compliance, with variance across patient groups according to age, social class, or work status.
At present, the four devices examined in our survey (pMDIs, capsule-based, reservoir-based, and blister-based DPIs) are used with the vast majority of treatments prescribed.

We found that physicians across the groups and two countries (France and Turkey) concurred on the principal factors that make an ideal inhaler: ease of use/handling; control of dose taking; portability; and multi-dose system. An in-depth evaluation of each of the four devices revealed a number of pros and cons for each and some suggestions for improvement were identified.

pMDIs are the preferred device for the treatment of acute attacks because of the minimal handling required, despite some difficulty in achieving effective drug delivery. Overall, however, capsule-based systems appear to be the most broadly acceptable across different patient groups, being intuitively simple to use and having the unique advantage of making the taking of inhaled medication a very tangible and reassuring experience. Potential improvements by developing multi-dose capsule-based devices with automatic loading to help improve patient convenience and compliance may take us one step closer to the ideal device by better fulfilling both clinical and patient needs.

REFERENCES

1. DPI Solutions – Perception of DPI system among doctors,Market Research Study by Vision Critical for Capsugel, January 2012.
2. Newman SP. Dry powder inhalers for optimal drug delivery. Expert Opin Biol Ther. 2004;4(1):23-33.
3. Atkins PJ. Dry powder inhalers: an overview. Respir Care. 2005;50(10):1304-12

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