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**The Influence of Dosage Frequency and Inhalation Device on Therapy Compliance in Asthmatic Patients**

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**Background:** The problem of non-compliance in daily practice, is still being underestimated. It is suggested that an important factor in non-compliance is the dosage frequency of a drug. Another factor of influence could be the kind of inhalation device (autohalor/dosisaerosol)

**Methods:** In a randomised controlled trial with 57 subjects the quotient of used and prescribed medication quantity was being measured. Each subject, during six weeks, daily used three inhalators (see Table 1). In this way it was possible to compare, within patients, the compliance with different inhalation devices and different dosage. A t-test was used to see if there was a difference in mean-compliance quotient of aerosol and autohalor. Patients were unaware that the medication was weighted before and after the study.

**Results:** The mean compliance quotient of the three devices used is 77.63% (SD = 24.77; range: 14.77-124.28%).

Table 1. Compliance with prescribed quantity of medication

	Inhalator		
	1	2	3
Device	autohaler	autohaler	aerosol
Daily doses frequency	2	4	2
Mean compliance quotient	80.69%	69.12%	83.09%

The mean compliance with inhalator 2 (higher daily doses frequency) is significantly lower than the compliance with inhalator 1 (11.5% difference, p = 0.001) and inhalator 3 (14.0% difference, p = 0.001). There appears to be no difference between the mean compliance quotient of the dosis-aerosol and the autohaler.

**Conclusion:** The mean compliance quotient in this study is 78%. Literature shows a great variability in compliance, spreading from 4 to 93%. In this study there seems to be no influence of the inhalation device in the compliance. The compliance with an inhalator with a daily doses frequency of four is significantly lower than with the inhalators with daily doses frequency of two. A high daily doses frequency seems to be of negative influence on compliance.

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**Does the Chronolog Actuator Affect the Emitted Dose and Aerosol Characteristics of Tilade MDI?**

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The Chronolog (Medtrac Technologies, CO) is a microprocessor monitoring device for metered dose inhalers (MDIs) used to measure patients' compliance with taking prescribed medication, logging the date and time of the MDI actuation. The current design of the Chronolog requires that the MDI be removed from its native actuator mouthpiece and used with the mouthpiece supplied with the Chronolog. As the actuator design affects the quality of the spray, it should be confirmed that the drug dose delivered per actuation and the aerosol size remain unchanged to ensure the same patient dose with the Chronolog. To demonstrate equivalence, emitted dose (ED) and particle size were measured for 3 canisters of Tilade ± Chronolog. The Anderson 8-stage cascade impactor (ACI) was used as the primary sizing method, and the stage contents assayed chemically for nedocrimal sodium (NS) using UV absorbance at 255 nm. The Aerosizer time-of-flight sizing system (API, MA) was the second sizing method. ED was measured by unit dose sampling apparatus for 15 individual actuations per canister. **Results:** A high variability in ED and ACI size distributions was observed between Tilade canisters with their native actuators (p < 0.001). With the Chronolog, there was a 9% decrease in ED (p = 0.001), a small (6%) but significant decrease in the MMAD (3.98 ± 0.19 µm vs 4.21 ± 0.17 µm, p = 0.006) and no change in the GSD. The fine particle fraction (FPF) i.e., % particles > 5.8 µm, was also unchanged. Whether the decrease in ED would alter the clinical outcome with use of the Chronolog with Tilade is unlikely, but not known. Similarly, the particle size changes were small and would be unlikely to alter deposition of NS in the lung when using Tilade with the Chronolog. The results with the Aerosizer were the opposite to those obtained using the ACI: MMAD increased with the Chronolog (p > 0.001) and FPF decreased. Differences may have been due to the need to excessively dilute this highly concentrated aerosol (2 mg NS/dose) for accurate sampling with the Aerosizer. While the resolution of the Aerosizer is greater than for the ACI, the latter technique has the advantage of quantitating the amount of drug per size range in absolute terms. As the ACI is currently regarded as the "gold standard", these results should be the primary ones quoted in this comparison. In conclusion, it appears that the dose/puff and particle size characteristics of Tilade MDI are minimally changed when actuated through the Chronolog and should not affect the treatment outcomes for patients using this device.

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**Ability of Patients, Nurses and Physicians with Aerosol Inhalation from MDI. A Multicentric Study**

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**Introduction:** The dependence of successful drug delivery from MDI on the inhalation technique (IT) and the frequent observation of faulty IT in patients (P) and physicians (Ph) are well documented facts. Claims for better instruction of P, nurses (N) and Ph have frequently appeared in the related literature for the last 2 decades. **Objective:** To evaluate the correctness of IT in a country-wide sample of P, N and Ph -all of them familiarized with the use of MDI-. in order to define adequate educational goals for the present time. **Methods:** Subjects were recruited among P, N and Ph from 12 health care centers of 12 Spanish cities spread around the country. A total of 1640 volunteers performed a practical demonstration of their IT with a placebo MDI in the presence of one of 12 trained observers, who evaluated the IT by means of a 10 items check list. The score of each item was weighted according to its relative importance, to add up a maximum total of 100 points for a "correct" IT. A difference of 30 points was considered clinically relevant. IT proficiency was correlated with age, years of MDI use, medical specialty (only for Ph) and medical center. The table shows the main **Results:**

	Patients	Nurses	Physicians
Subjects (% of total)	746 (46)	466 (28)	428 (26)
Mean Score (SD)	62 (26)	71 (22)	77 (23)
Most Frequent Errors (% subjects):			
• Inspir. & firing not coordinated:	42.9	42.5	29.9
• No post-inspiratory apnea:	56.2	44.2	34.8
% Subjects with 100 Points	8.9	14.6	27.8

**Conclusions:** Ability to use of MDI in patients and medical personnel is limited. Despite the physicians awareness on the IT in the use of MDI, this study shows important deficiencies, particularly in the most determinant aspects of the inhalation maneuver that require deep changes in educational efforts.

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**The Efficacy of Salbutamol Administered from a New Metered Dose Powder Inhaler Compared with that of a Metered Dose Inhaler with a Spacer**

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The aim of the study was to compare the efficacy of one dose (0.1 mg) of salbutamol inhaled from a new metered dose powder inhaler (Leiras MDPI) with that of one dose (0.1 mg) of salbutamol from a conventional metered dose inhaler attached to a spacer device (MDI + S).

A new MDPI has been developed by Leiras Oy to meet the requirements of reliable and accurate dosing, high number of respirable particles (< 5.8 µm), low oropharyngeal deposition of the drug, and more convenient handling compared with those of MDIs connected to a spacer. Leiras MDPI is preloaded with 200 doses of salbutamol powder. The respirable fraction is ca. 50% of the delivered dose.

This was a two-day, cross-over, double-blind, double-dummy and placebo-controlled multicenter study. Forty-two asthmatic outpatients with the baseline FEV<sub>1</sub> 35-70% of predicted were randomly divided into two groups of equal size. On the first day group I inhaled 0.1 mg of salbutamol from an MDPI and placebo from an MDI + S, and on the second day placebo from a MDPI and 0.1 mg of salbutamol from an MDI + S. With group II the procedure was completed vice versa. Pulmonary function (FEV<sub>1</sub> & R<sub>aw</sub>) was measured during 6 hours after drug application and compared with predose values.

Thirty-three patients completed the study according to the protocol. The baseline FEV<sub>1</sub> was identical on both study days (1.97 L). With MDI + S the mean increase in FEV<sub>1</sub> was 39% (0.77 L), and with MDPI also 39% (0.77 L). The baseline R<sub>aw</sub>-values were 0.74 kPa · s · L<sup>-1</sup> and 0.65 kPa · s · L<sup>-1</sup> for MDI + S and MDPI, respectively. The observed decline in R<sub>aw</sub> was also of similar magnitude; 52% (0.38 kPa · s · L<sup>-1</sup>) and 47% (0.30 kPa · s · L<sup>-1</sup>) with MDI + S and MDPI, respectively.

In conclusion, Leiras MDPI appears to be as efficient a device as a conventional pressurised MDI attached to a spacer in administering salbutamol in the treatment of asthma.

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**Bronchodilator Response to Drug Administration from an Actuator Alone or Spacer Devices**

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Spacer devices are extensions to metered-dose inhalers designed to eliminate the need for hand-breath co-ordination which reduce the deposition of large aerosol particles in the oropharynx. In three groups of asthmatics not trained to the use of MDIs, we evaluated the efficacy of a salbutamol-containing aerosol preparation administered by a trained staff from either the actuator alone (group I), or