What do you get when you cross the border and buy albuterol inhalers for a fraction of the US cost?

A comparison of pharmaceutical quality and product performance of inhalers obtained in Mexico to those available in the US

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Objective

The purpose of this study is to provide some reasonable expectations for a medical tourist who shops in Mexico for albuterol MDIs or for providers who encounter such a patient by comparing pharmaceutical quality and product performance of the consumer available brands.

Background & Literature Review

American asthmatics pay three to five times more for their inhalers than patients in other countries. And, due to the repatenting of albuterol rescue inhalers when the eco-friendly hydrofluoroalkane (HFA) propellant was implemented, the price of this brand-only, asthma-essential medication is now $30 to $100, much higher than the $15 people paid for generics ten years ago.1,2 There is no telling when inhaler cost will decrease in the US because complicated patents for pumps, drug delivery technology, and manufacturing procedures have unexpectedly stalled generic availability and rendered release dates unpredictable.3,4

Medical tourism is a term that is used to describe the international border-crossing for healthcare products and services. American residents go to Mexico to purchase medical services, dental services, and medications. Many prescription-only drugs in the US are available for purchase at the border-town Mexican pharmacies without prescription requirements and, for lower cost. Since the price tag on albuterol inhalers in Mexico is estimated to be 1/3 to 1/5 of that in the US, it is no wonder that lower cost is the most common explanation offered by healthcare border crossers.5,6

The question remains: what do you get when you cross the border and buy medications, such as albuterol metered-dose inhalers (MDIs), for cheaper price?

Several studies have compared pharmaceutical quality of medications that were available in Mexico or other countries and showed varying results. Particularly, with respect to albuterol inhalers, a bioequivalence study of two brands of albuterol inhalers, manufactured in Mexico, VentolinHFA and Assal®2, were clinically different despite both were expected to deliver 100 μg of drug per puff. VentolinHFA exhibited higher forced expiratory volume in 1 second (FEV1) values, higher maximum effect (E∞), higher time to E∞, longer half-life and higher area under the response-time curve (AUC) than Assal®. If two albuterol brands labeled with the same dose are clinically different in every pharmacodynamic parameter examined, what other differences might we find among inhalers available in Mexico when we include more brands and analyze pharmaceutical qualities such as respirable mass?

Methods

Visual Inspection

All five inhaler brands were sold in a Spanish-labeled box containing a single page instruction manual. Each inhaler label had a visible lot number, expiration date, and 100 mg price tag. The manufacturing location included China, Mexico, India, and Spain (Table 2). Two brands showed a pictorial pregnancy warning label. Sacrusyt’s actuator was the only one with an unusually shaped mouthpiece. Most of the MDIs were purchased for about $3 to $5. Ventolin was the most expensive of all, the units used in the study were purchased for $10 but they were sold for $15 or $20 at other pharmacias locations. The inhaler labels all exhibited what appeared to be product weight; however, to what each weight was referring was not precisely apparent. What weighs 20 g in the Victory box? We could speculate all day but the answer is unknown. Also vexing is why some are listed in milligrams and some in grams.

Data and Analysis

The measurements of total dose and respirable mass among the five Mexican purchased brands were varied and are presented in Figure 1 alongside that of Proventil and Ventolin purchased in the US (“US Proventil” and “US Ventolin”). The study’s MDI2 averages ranged from 57 μg (Assal) to 75 μg (Xeneric), while the average total dose of the US Proventil was 82 μg and was 79 μg for US Ventolin. It was not surprising that the US-purchased MDIs exhibited higher average total albuterol because they were labeled to contain 108 μg albuterol per actuation, which translated into 90 μg albuterol, while the study MDIs were labeled to have 100 μg dose, which translated to 83 μg albuterol (assuming the salt form is also albuterol sulfate). In general, the respirable mass of the non-US MDIs did not appear quite as different from that of the US brands as they did with regard to the total dose. Among the study MDIs, respirable mass ranged from 28 μg (Ventolin and Xeneric) to 41 μg (Victory), which compares to 42 μg (US Proventil) and 38 μg (US Ventolin) in Figure 2.

To further investigate the variability among the non-US purchased brands, student-tests were performed. Total dose and respirable mass data from each of the five brands were examined against that of the other four brands (20 comparisons total). All comparisons exhibited significant difference (p<0.05) except the study MDIs and US versions of Ventolin and Xeneric, the US versions of the other MDIs and the Assal®. We cannot tell, however, is what the clinical significance is with regard to any differences found among the study MDIs or any differences that appeared between the non-US purchased and the US purchased MDIs.

Table 1. Findings Among Sample Brands NOT Significantly Different

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<thead>
<tr>
<th>Total Dose</th>
<th>Respirable Mass</th>
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<tbody>
<tr>
<td>Sacrusyt vs Ventolin (p=0.84)</td>
<td>Sacrusyt vs Assal (p=0.89)</td>
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<tr>
<td>Victory vs Assal (p=0.28)</td>
<td>Xeneric vs Assal (p=0.98)</td>
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<th>Table 2. Visual Inspection</th>
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<td>Brand</td>
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<tr>
<td>Victory</td>
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<td>Assal</td>
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<td>Sacrusyt</td>
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<td>Xeneric</td>
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<td>Ventolin</td>
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Figure 1. Mexican Salbutamol MDI Samples

Figure 2. Mean Total Dose and Respirable Mass, μg

Table: Data Results & Analysis

Limitations

There were several limitations to this investigation:

• Only manufacturers included in study were ones available to purchase in stores in Nogales, Mexico.
• Unable to determine the exact number of Sacrusyt inhalers upon subsequent visits to Nogales to purchase inhalers.
• We were not equipped to determine if the samples were HFA or HFC.

Table: Data Results & Analysis

Conclusion, Discussion, & Recommendations for Future Research

Previous bioequivalence research determined significant pharmacodynamic differences among albuterol MDIs available in Mexico (Ventolin superior to Assal). In this pharmaceutical examination of these products, we also found significant differences between Assal and Ventolin. While Ventolin had higher total dose, Assal was superior in respirable mass. Thus, this data cannot fully explain the differences in patient response to each brand found in the previous study.

Patients who are medical tourists and practitioners who serve this population should be wary of the high variance discovered between the brands and between the US purchased and US-purchased MDIs. Sixteen of the twenty patients indicated differences between the sample brands against each other were significantly different in total dose and respirable mass. This indicates that a patient who has used US MDIs before can’t necessarily expect to get the same dose from non-US brands. Furthermore, even though the labeled dose is the same, patients cannot expect consistency in total dose or respirable mass between one non-US MD and another.

Further investigation is needed to determine the albuterol salt form and to determine if these inhalers are HFA or chlorofluorocarbon (CFC). Also, Xeneric, Sacrusyt, and Victory have not yet been examined in a bioequivalence study and it would be interesting to see how they fare in light of their pharmacological differences.

References