WORKING PAPER

Pilot Assessment of the Quality of Ciprofloxacin in selected Latin American Cities

The research was overseen by Roger Bate, Director of the Safe Medicines Coalition. The sampling collections and medicine testing were funded by the Legatum Institute and the International Policy Network.

Summary

Ciprofloxacin was sampled from pharmacies in ten Central and South American cities. At least six per cent of the medicines are substandard or falsified. Sao Paolo, Buenos Aires and Montevideo have very few substandard or falsified medicines, whereas Asuncion and Caracas had considerably more. There are possible explanations for this, such as the latter cities having more unregistered products sold in pharmacies, but this is only a pilot study, without detailed analysis of the possible socioeconomic and legal causes. The study also only assesses a few cities and one medicine, a more detailed assessment would be useful to guide policymakers as to how to respond to this public health menace.

Introduction

There have been assessments of basic medicine quality from many countries and regions across the world (IOM 2013), but almost none in Central and South America. Over the past decade my colleagues and I have collected over ten thousand samples of medicines from 22 cities in emerging markets, but the only one from the Latin region was Sao Paolo in Brazil. We have now rectified this gap, at least for one critical medicine, the broad spectrum antibiotic ciprofloxacin. We have undertaken considerable research on Cipro before (Bate et al 2015, Bate et al 2016), and it is the one drug we have found in every city and most pharmacies within each city. We therefore expected to be able to find it in each of the nine Latin cities (in addition to Sao Paolo) we sampled, which included Asuncion, Buenos Aires, Caracas, Guatemala City, Guayaquil, La Paz, Lima, Montevideo, Sao Paolo and Tegucicalpa.

We are interested in identifying fake or falsified medicines, those that are not made by the manufacturer on the packaging, and assessing where such products occur. But our main aim is to analyze the quality of medicines made by the legitimate manufacturer. This is because our prior research indicates that, at least in emerging markets, substandard medicines are the larger threat and one that is arguably easier for policymakers to address. As such the aim of this paper is to identify any substandard medicines in each city, assess where they are made, and whether they are registered in the country of purchase. The findings will therefore be comparable with prior research, but novel because most Latin countries have never been assessed in this way.

Method

We instructed covert shoppers from the region to randomly walk into pharmacies and claim that a family member needed a specific type of drug. To mimic real patients as much as possible, the covert shoppers did not present a doctor's prescription and always purchased the pharmacist-suggested brand. Informal drug vendors (bus vendors, mobile carts, etc.) occur in some locations, but to be able to compare across all locations, our shoppers only visited pharmacies with a regular storefront. As a result, our samples are likely to understate the problem of poor-quality drugs, given the expectation and existing evidence that informal vendors sell worse drugs (IOM 2013).

All medicines were assessed following the Global Pharma Health Fund (GPHF) e.V. Minilab® protocol to identify substandard or falsified medicines (Jahnke et al, 2001). The key test for our sample is the semi-quantitative thin-layer chromatography (TLC), which assesses the presence and concentration of active ingredient in a test sample as compared to the reference standard. A sample is referred to as falsified if it contains zero correct API , and referred to as substandard if it contains some correct API but the amount of API is under-dosed (below 80%). This technique has been used for the past decade by our team in every sampling. All tests were conducted within 60 days after purchase, following the classification in Bate, Jin and Mathur (2015).

It is important to note that medicines can be substandard and still pass TLC, since they may not be soluble or be poorly formulated in other ways. As a result our assessments are likely to underestimate the number of poor quality medicines.

As acknowledged in other studies (Attaran et al 2012), the legal distinction between falsified and substandard products is one of intention: both sorts of compromised medicines are not as labeled and violate the relevant technical standards, but substandard medicines are compromised accidentally or negligently, while falsified medicines are compromised intentionally, with this difference not always being apparent from the content of the medicine. In other words, legally speaking, falsified products are the product of organized criminal intent, but substandard medicines are wrongfully produced by otherwise legitimate, law-abiding manufacturers. However, this legal distinction breaks down when a legitimate manufacturer intentionally cheats on the ingredients of the medicine. In light of the difficulty to detect the intent of manufacture, this paper distinguishes substandard and falsified drugs by API only.

Results

As table 1 below shows, 513 samples of ciprofloxacin were bought in ten cities (Sao Paolo was sampled twice, the first time in 2012). Overall 6.3% (33/518) of the medicines fail basic quality, of these ten (1.9%) were obvious fakes and 23 (4.4%) were substandard.

Five cities had no obvious fake medicines, Ascuncion (4/54 7.4%) and Caracas (2/42 4.7%) had more fakes than the other cities. Only Buenos Aires had no failing medicines at all (no falsified medicines and no substandards). Caracas had the most substandard medicines (4/42, 9.5%).

Table 1

City	Samples	Total failing	Fake	Fail %	Fake %	% Substandard	Registered	% Registered
Sao Paolo 2012	70	3	1	4.28	1.43	2.86	66	94.28
Sao Paolo 2016	42	1	0	2.38	0	2.38	41	97.62
Guayaquil	43	2	0	4.65	0	4.65	38	88.37
Lima	55	4	1	7.27	1.82	5.45	50	90.91
Tegucicalpa	44	3	1	6.81	2.27	4.54	37	84.09
Guatemala City	52	4	1	7.69	1.92	5.77	44	84.61
La Paz	33	2	0	6.06	0	6.06	30	90.91
Ascuncion	54	7	4	12.96	7.40	5.55	38	70.37
Buenos Aires	44	0	0	0	0	0	41	93.18
Montevideo	39	1	0	2.56	0	2.56	37	94.87
Caracas	42	6	2	14.28	4.76	9.52	29	69.05
	518	33	10	6.37	1.93	4.44	451	87.06

Removing the ten fake medicines from the sample, where by definition we do not know where they were made, the location of production of the legitimate medicine is in table 2 below. The largest supplier of Cipro to all Latin countries is India, providing 35% (179/508) of the sample. Products made in Latin America (whether made domestically in the country of purchase or imported) provide 159 (31%) samples and Europe, US and other OECD nations provide the next most at 90 (18%). OECD medicines did not fail at all, whereas Indian and Chinese medicines both failed more than other locations at over 6% of the sample.

Approximately 87 per cent of the medicines were registered in the country in which they were procured, but this belied a range of 97% in Sao Paolo down to 70% in Caracas and Asuncion. The sample sizes are too small to determine statistically whether unregistered products failed more often, however, in Caracas three of the four substandard products were indeed unregistered.

Table 2

Production location	Samples	Substandards		%fail
Domestic	71	2		2.81
India	179	12		6.70
China	80	5		6.25
OECD	90	0		0
Other Latam	88	4		4.54
	508	23		4.52

Discussion

It is interesting to compare these new results with previous results from prior papers. In our largest study of ciprofloxacin (Bate et al 2015) we found that 83 out of 1437 samples of Cipro, roughly 5.8% of samples, were substandard. This is a slightly higher percentage than found in this latest research (4.5%). The discrepancy is most likely explained by the fact that just over 8% of the sample bought in African cities failed, whereas the rate was closer to 4% in mid-income emerging markets (including Indian cities and the original Sao Paolo sample of 2012). In that respect these new data are consistent with previous data.

Also consistent, though not analyzed in detail, is that richer cities tend to have better quality medicines, as we saw in Bate et al 2015 and Bate et al 2016. Buenos Aires, Sao Paolo and Montevideo are among the richer cities and Asuncion and Caracas among the poorer and their quality results reflect that. Asuncion and Caracas also have the fewest registered products, and previous research (Bate al 2015 and Bate et al 2016) shows that unregistered products are more likely to fail quality control and such nations are associated with more falsified medicines.

In summary, Latin American cities have more registered Cipro and it is of better quality than African cities, but marginally worse results by comparison with other mid-income nation cities analyzed previously.

Conclusion

Ten Central and South American cities had ciprofloxacin sampled from local pharmacies. Approximately 6.3% failed a very basic quality thin layer chromatography test, providing a minimum assessment of substandard and falsified ciprofloxacin medicines on the market. There was quite a variety in performance of the cities, with Sao Paolo, Buenos Aires and Montevideo have very few substandard medicines, whereas Asuncion and Caracas had considerably more.

This is only a pilot study looking at a few cities and one medicine, a more detailed assessment would be useful to guide policymakers as to how to respond to this public health menace.

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