Misoprostol and declining abortion-related morbidity in Santo Domingo, Dominican Republic: a temporal association

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Objective To validate anecdotal reports that abortion-related complications decreased in the Dominican Republic after the introduction of misoprostol into the country.

Design Retrospective records reviews and cross-sectional surveys, interviews and focus groups.

Setting Family planning clinics, pharmacies, door-to-door canvassing and a tertiary care maternity hospital in Santo Domingo, Dominican Republic.

Population Women of reproductive age in Santo Domingo, Dominican Republic.

Methods Qualitative and quantitative methods were used. Individual interviews and focus groups of reproductive health professionals, non-governmental organisation leaders and women’s group leaders (n = 50) were conducted to discover the role of misoprostol in the Dominican Republic. Local women (n = 157) were surveyed to determine their knowledge of misoprostol as an abortifacient and mystery client visits were made to 80 pharmacies in order to purchase misoprostol without a prescription. Sales data were obtained that documented when misoprostol was introduced to the Dominican Republic pharmacies. Hospital admissions for abortions from the prior eight years were reviewed and hospital emergency room consultation ledgers of 31,190 visits for the period 1994–2001 were reviewed for abortion complications.

Main outcome measures Frequencies of maternal morbidities and knowledge of misoprostol.

Results Mystery clients purchased misoprostol without a prescription in nearly 64% of pharmacies; staff provided little additional information or counselling. Reliable sales data documented the introduction of misoprostol in 1986. Abortion complications decreased from 11.7% of abortions in 1986 to 1.7% in 2001. The majority of professionals interviewed felt that knowledge of these findings should be made public.

Conclusions The data were of too poor quality to validate the verbal reports reliably, but misoprostol appears to have been widely used over a period when abortion-related morbidity fell. It remains plausible that the use of misoprostol contributed to the reduction.

INTRODUCTION

Globally, of the estimated 46 million induced abortions that take place annually, perhaps 20 million are performed under illegal and unsafe conditions.1 In Latin America, where law often prohibits access to safe abortion, nearly 800,000 women are hospitalised each year with abortion complications.2 For example, in 1992 in the Dominican Republic, where abortion is illegal, 16,500 Dominican women were hospitalised for abortion-related complications, and one-fifth of maternal mortality in the nation’s capital, Santo Domingo, was attributed to unsafe abortion.3

Wherever safe, legal abortion is not readily accessible, women resort to abortifacient drugs; some of the herbs and medicinals women use to end pregnancy fail to work, while those that are more effective may have dangerous side effects. Misoprostol, a synthetic analogue of the prostaglandin E1, was originally produced for the prevention of gastrointestinal (GI) ulceration but provides an effective alternative to other substances used for abortion. In many European Union countries and in the United States it is used
for medical abortion either alone or in combination with mifepristone (RU486). Oral or vaginal administration of the drug during pregnancy results in cervical dilatation, uterine contractions, uterine bleeding and often, depending on the dose and the duration of the pregnancy, complete abortion.\(^\text{8}\) While 80–90% of patients tolerate the drug well, the reported side effects include cramping, nausea, vomiting, diarrhoea and fever,\(^\text{5}\) all of which are dose dependent and reversible. The risk of uterine rupture, likewise dose dependent, increases with increasing gestational age. A retrospective study reported congenital abnormalities in children born to women who had used misoprostol,\(^\text{9}\) but a prospective study of 86 misoprostol-exposed pregnancies showed no difference in the prevalence or type of birth defects when compared with 86 matched controls.\(^\text{7}\)

The use of self-administered misoprostol to terminate pregnancy was first documented in Brazil. Introduced to the Brazilian market in 1986, misoprostol was shown to be associated with fewer abortion complications than were other methods of clandestine abortion. Following government restrictions limiting the availability of the drug in 1991, one Brazilian city experienced both increased abortion-related morbidity and a tripling of maternal mortality.\(^\text{8}\)

Anecdotal reports have suggested that increased access to misoprostol has also changed the face of Dominican abortion practice. As one obstetrician, interviewed in a local newspaper, stated, ‘Since, Cytotec became available, the hospital rarely has to treat women for complications resulting from abortions performed in substandard clinics’.\(^\text{8}\) Our study sought to validate these anecdotal reports of changes in Dominican abortion outcomes as similar to those documented in Brazil, and to investigate the potential of misoprostol as a means of harm reduction in the historical context of unsafe abortion practices in Santo Domingo.

## METHODS

A variety of methods were used to assess a temporal association between the introduction of misoprostol and changes in abortion-related complications. Qualitative individual interviews and focus groups, a knowledge survey of women and mystery client visits were conducted to assess the prevalence of knowledge about misoprostol’s use as an abortifacient and the availability of misoprostol without a prescription in Santo Domingo pharmacies. Because of the sensitive nature of abortion in Latin America in general and in the Dominican Republic in particular, key informants were also questioned about the potential effects of publishing the results of this study on the availability and safe use of misoprostol by Dominican women. Hospital emergency room consultation ledgers were reviewed and the numbers of abortions and abortion-related complications tallied. Sales data since the introduction of misoprostol to pharmacies in the Dominican Republic were obtained.

A total of 50 key informants were interviewed using both individual interviews (\(n = 23\), all senior physicians and nurses) and focus groups (\(n = 4\), with a total of 27 participants: one group of senior physicians and nurses, one group of senior residents, two focus groups of medical students and vocational nurses and one focus group of women’s health experts working for local non-governmental organisations (NGOs). The key informants were 18 doctors (obstetricians, general practice physicians and gastroenterologists), 12 nurses, 14 medical students, 5 interns and residents, 2 hospital directors and staff of reproductive health (6) and women’s health governmental (5) and non-governmental organisations (12). They were asked three open-ended questions about their opinions of misoprostol, its impact on women’s health in the Dominican Republic and the potential consequences of publishing the results of this study of its use. The key informants were selected based on their knowledge of reproductive health, availability and by snowball referrals. The interviews were conducted in Spanish by a Dominican obstetrician gynaecologist and women’s health specialist. The responses were audiotaped and transcribed and then analysed using content analysis by two of the authors.

The responses from the key informant interviews were used to help refine a draft questionnaire to assess Dominican women’s knowledge of misoprostol, its abortifacient properties, availability and side effects. The questionnaire was administered to a convenience sample of 157, recruited via door-to-door canvassing in the working class neighbourhoods of Santo Domingo served by the local public health service maternity hospitals (\(n = 105\)) and from the family planning clinic waiting rooms of Santo Domingo’s two largest public health maternity hospitals and local women’s clinics (\(n = 52\)). The questionnaire was administered face-to-face and read to each respondent in Spanish by a Dominican researcher.

Five Dominican members of the research team visited a convenience sample of 80 pharmacies in Santo Domingo. The pharmacies were selected based on their location in different socio-economic ‘barrios’ or neighbourhoods. The mystery clients comprised a young (21 years old) male–female couple, a man alone and two women, each alone. They entered the pharmacies and attempted to purchase misoprostol without prescription.

To assess the number of abortion complications before and after the introduction of misoprostol, emergency room consultation ledgers from the two largest public health maternity hospitals were reviewed. These ledgers were difficult to locate, and, when found, had significant paper damage from water, moths and rodents. There were major losses at one of the hospitals, Maternidad Alta Gracia, due to hurricane destruction of the records’ room. No primary records for either hospital were available for the year 1986, the year misoprostol was allegedly introduced, and no complete records were available for any single year.

Records were organised into hand-written ledgers with approximately one month of emergency room consultations per ledger book (range 26–45 days). The years 1994, 1996, 1999 and 2001 were chosen for analysis because surviving, legible data were available from both hospitals for these years and because they represented roughly equally spaced data points throughout the eight-year period for which the data were available (1994–2001, data collection occurred in December of 2002). To minimise the potential effect of seasonal variation on the rate of abortion or its complications, only months with viable records for all four years were analysed. Thus, the ledgers that correlated with January, June and September were analysed in their entirety.

Ledgers were reviewed by two of the authors, a statistician and an MD/MPH student. They examined each entry and all consultations related to abortion (including the diagnoses of abortion, incomplete abortion, inevitable abortion, induced abortion, completed abortion, retained products of conception, missed abortion and pregnancy plus dilation and curettage), and its potentially serious complications (defined as infection, uterine perforation, haemorrhage and abortion with severe anaemia) were manually tallied. Infected abortion and septic abortion were combined as ‘infection’. The rate of abortion complications was calculated as the number of the above-defined complications divided by the total number of abortion-related consultations.

As hospital ledgers were not available for the period before 1994, once we verified that misoprostol was introduced to the Dominican market in 1986, we sought secondary sources for baseline data against which to compare our tabulated rates. Historical comparison data were provided by a doctoral thesis by Figueroa et al.,10 which retrospectively reviewed 8199 obstetric and gynaecological encounters at Maternidad San Lorenzo de los Mina from August to October 1986. The study documented the number of abortions and the number of abortion complications (defined as infection, uterine perforation, haemorrhage, severe anaemia or retained products of conception) for this period. All but the final complication listed were directly comparable with our diagnoses of interest. Because this baseline information was available only for Maternidad San Lorenzo de los Mina, we only used the tabulated data from this hospital (n = 31,190 reviewed emergency room consultations) in our analysis.

All data were entered into Microsoft Excel spreadsheets and exported into Stata 8.0 (StataCorp, College Station, Texas). The results were analysed using χ² and Fisher’s exact tests. A P value of <0.05 was considered significant.

The University of California, Berkeley Committee on Human Research, the Dominican Ministry of Health (SESPAS) and the participating hospitals’ Institutional Review Boards approved the protocols used in this study. All participants gave verbal informed consent after hearing a full explanation of the study, risks and benefits.

**RESULTS**

The 50 key informants responded uniformly to the question: ‘When was misoprostol introduced into the Dominican Republic?’ They stated that introduction occurred around 1986, with widespread use by 1994. Further, most stated that misoprostol is now used for the majority (perhaps up to 90%) of induced abortions. One-third of informants thought that the availability of misoprostol had improved women’s health, as these quotes from the key informant interviews demonstrate:

We haven’t seen a single death from illegal abortion, and before there were four or five deaths per year. The business of illegal abortion has disappeared because now they (women) come to the hospital . . . but the incidence of abortion has not changed, the social and economic factors are the same as before, the only change is that now there is misoprostol. The impact is that the maternal death associated with abortion has dropped.

It is the panacea of Obstetrics! It has resolved many of the complications related to abortion. Septic abortion has disappeared.

Twelve percent said they thought the drug had a negative effect;

They say there have been cases where the babies have been born with malformations.

It is not good that adolescents use this without the control of the sales.

The rest were neutral or stated that they were confused.

In general, those who reported that the effect was positive compared previous high rates of maternal morbidity and mortality due to abortion complications with lower rates found today, while those who felt the drug had a negative effect cited fear of complications and concerns that women would use misoprostol-induced abortions instead of using recognised family planning methods.

On the whole, obstetricians and gynaecologists, senior nurses and NGO leaders welcomed the drug. Those who voiced a negative opinion about misoprostol (n = 6) also stated that they objected to abortion. Twenty-two percent of informants reported observing uninformed or excessive (up to 10 tablets at one time) use. Sixty percent supported our investigation of misoprostol use and publication of the results as a means of improving abortion-related outcomes; those who opposed publication of results often stated a religious reason or feared retribution and stricter control on misoprostol sales:

In a Christian community, we have to be careful about the Church, but the use of the drug has definitely reduced maternal mortality . . . so what do we want: to allow women to die or to let them use it [misoprostol]?

They should legalize its use. The only negative impact that can come from the results of this report will be with the Church.

The Dominican gastroenterologists (n = 2) and other physicians were asked if misoprostol was being used for GI as well as obstetric purposes. They stated that misoprostol was rarely prescribed for GI symptoms, having been replaced by proton-pump inhibitor (PPI) drugs. It was widely accepted by our key informants that the majority of misoprostol sold in the Dominican Republic since the mid to late 1990s are for the off-label use to induce abortions, with the remainder being used legally, but again off label, to induce labour in term gestations and in cases of fetal demise.

The women surveyed (n = 157) were a convenience sample recruited in family planning clinics and by door-to-door canvassing in Santo Domingo. They were primarily lower and middle class residents of Santo Domingo (Table 1).

Three-quarters (n = 117) had ‘ever heard’ of misoprostol and the following statistics refer to these women. Ninety-three percent were aware that the drug could induce abortion. Ninety-one percent had heard of misoprostol through friends, family members, neighbours and co-workers; 7% had heard about misoprostol from a doctor, health worker or pharmacist; and 3% learned about the drug from television or the media. Two-thirds of those familiar with the drug knew where to obtain it, and 60% said it was available without prescription. One in 20 said it could be purchased on the ‘black market’, or that fraudulent prescriptions could be obtained from medical students and auxiliary nurses.

Half of those who had heard of the drug were unaware of any potential risks or serious side effects to its use. One-quarter of those mentioning side effects reported symptoms such as nervousness or infertility, which are not recognised in the scientific literature to be associated with misoprostol use.

Of the 80 pharmacies visited, 64% (n = 51) were willing to sell misoprostol without a prescription. Generally the person making the sale was a salesperson or pharmacy technician and not the pharmacist. The pharmacy location based on socio-economic status (SES) of the neighbourhood as judged by the Dominican members of the team were 15% (12) high income, 2.5% (2) medium income and 83% (66) low income or, as it is called in the Dominican Republic, ‘clase popular’. Sales were more common in the low income neighbourhoods (70% vs 19% sales, \( P < 0.005 \)), while in higher socio-economic areas investigators were more likely to be referred to a doctor (33% vs 8%, \( P = 0.02 \)).

The mean price quoted was approximately US$1.00 per 200-µg tablet. The modal recommended dose was four tablets (range 1–10). Pharmacy staff provided little additional information and no counselling on proper use or follow up. Eighty percent (n = 41) of the time no one advised the purchaser to seek medical care for heavy bleeding; 9 out of 10 did not mention any risks or side effects. There was no association with SES of the neighbourhood and whether counselling or advice was given.

<table>
<thead>
<tr>
<th>Year</th>
<th>Units</th>
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<tbody>
<tr>
<td>1986</td>
<td>717</td>
</tr>
<tr>
<td>1987</td>
<td>1579</td>
</tr>
<tr>
<td>1988</td>
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<td>30,023</td>
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<td>1994</td>
<td>48,349</td>
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<td>1999</td>
<td>22,498</td>
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<tr>
<td>2000</td>
<td>26,752</td>
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</tbody>
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Fig. 1. Misoprostol sales in units (each unit consists of twenty 200-µg tablets).
The authors sought unsuccessfully to obtain information on the annual volume of misoprostol imported to or sold in Santo Domingo from both the Dominican government and the pharmaceutical industry. The sales data were purchased through IMS Health, a Web-based company providing sales data of pharmaceutical companies. Misoprostol (as Cytotec) was introduced in the Dominican Republic in June 1986 with annual sales of 717 units (each unit contained twenty 200 μg tablets). Sales of units increased annually, reaching a peak of 50,482 units sold in 1996, afterwards mean annual sales were in the 20–30,000 unit range (Fig. 1).

The percentage of abortion-related visits due to serious complications was lower in 1994–2001 than in 1986. These complications represented 11.7% of abortion admissions in 1986, but only 1.7% in 2001. This decrease in overall complications was mirrored by decreases in specific complications as well, as shown in Table 2.

**DISCUSSION**

As in Brazil, knowledge of misoprostol’s effect has spread through the Santo Domingo community by word of mouth. Many pharmacies make misoprostol available without prescription and ‘black market’ or street sales of the drug and its prescriptions are reported. However, information on appropriate dose and route of administration and necessary follow up for bleeding is incomplete or missing. Few women surveyed knew of potential side effects identified in the professional literature or of the need for medical follow up. To date, the formal health sector has played a minimal role in promoting safe misoprostol use or advancing the drug as a means of harm reduction. However, even without the support of the health sector, since the introduction of misoprostol in 1986 there has been a 75% decline in serious abortion complications at one of the largest maternity hospitals in Santo Domingo.

Whether the temporal association between misoprostol’s introduction in 1986 and the documented decline in abortion-related morbidity is causal is impossible to demonstrate with the current data. However, there are explanations for why misoprostol could affect abortion outcomes. First, many women who use misoprostol succeed in inducing complete abortion without further medical intervention (the rates of successful first trimester abortion using misoprostol alone reported in the literature range from 5% to 97%), thereby avoiding the well-documented risks of more invasive techniques of clandestine abortion. Second, abortion complications are known to rise rapidly with the duration of pregnancy, and research shows that the percentage of successful and complete abortion falls dramatically with increasing gestational age. It is possible that the increased access to abortion provided by misoprostol allows women to terminate their own pregnancies at a relatively earlier stage than they would have done if seeking an illegal abortion from a second party. Finally, for those women requiring uterine evacuation, the discrete nature of misoprostol encourages women who have initiated vaginal bleeding to seek medical care without fear of legal consequences.

This study has many limitations. First, official records regarding clandestine and illegal activities are inherently incomplete. The Dominican records that did exist were difficult to access and incompletely preserved. Second, annual sales data for misoprostol could not be stratified by intended use, thereby making correlation of variation in sales with changing abortion complication rates impossible. Undoubtedly, sales for GI uses contributed to the high volumes of misoprostol sold in the mid to late 1980s. However, the subsequent introduction and acceptance of the PPIs decreased GI-related use of misoprostol globally and in the Dominican Republic. Sales figures do document that misoprostol became available in Dominican pharmacies in 1986, and key informant interviews and secondary data sources do support that Dominican women were aware of the use of misoprostol for abortion induction. Widespread knowledge of misoprostol among women of Dominican descent living in New York was documented by Rosing et al. in the spring of 1999. Findings that misoprostol usage was more prevalent among women born in the Dominican Republic than women born in the United States, and that 40% of those surveyed reported ‘another country’ as their potential source for misoprostol, support the conclusion that misoprostol for induced abortion was known in the Dominican Republic at that time. Further, our survey revealed that many Dominican women do know about the abortifacient effect of the drug and how to obtain it. Taken together, these independently obtained data may support local health experts’ statements that misoprostol use for abortion induction became common at the same time that abortion complications began to decline.

Another limitation of this study was the use of convenience samples; such potentially biased sampling prevents direct generalisation of our results. However, the consistency of our findings is suggestive. The hospital studied was also selected based on ease of access. However, Maternidad San Lorenzo de los Mina is one of the largest maternity hospitals in the country, with 15,000 births annually.

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**Table 2.** Specific serious abortion complications—Maternidad los Mina.

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<tbody>
<tr>
<td>Number of abortion-related admissions reviewed</td>
<td>596</td>
<td>777</td>
<td>883</td>
<td>1326</td>
<td>648</td>
</tr>
<tr>
<td>Percentage of abortions with serious complications</td>
<td>11.7</td>
<td>4.6</td>
<td>1.5</td>
<td>2.1</td>
<td>1.7</td>
</tr>
<tr>
<td>Percentage of abortions with infection</td>
<td>4.0</td>
<td>3.1</td>
<td>1.4</td>
<td>0.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Percentage of abortions with haemorrhage</td>
<td>7.2</td>
<td>1.2</td>
<td>0.0</td>
<td>0.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Percentage of abortions with uterine perforation</td>
<td>0.5</td>
<td>0.4</td>
<td>0.1</td>
<td>0.1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

* 1986 data from Figueroa et al.10

11% of births in the entire country and 28% of the total births in the Santo Domingo national district.\textsuperscript{16}

Finally, there are limitations to the comparison of the hospital ledgers to the baseline, secondary data. Although we were fortunate to find the secondary data from Figueroa et al.\textsuperscript{10} to use for comparison, we cannot independently confirm the accuracy of this secondary source. The study does use similar methods to ours (retrospective analysis of abortion-related encounters with tallied numbers of abortions and abortion complications), and it represents the only surviving source of data on pre-misoprostol abortion complications at Maternidad San Lorenzo de los Mina.

Globally, particularly in developing countries, there is a paucity of information on the subject of complications related to clandestine abortions and the potential influence of new technologies to decrease maternal morbidity; we hope that our analysis will inspire additional research in the field. The potential of medical abortion with misoprostol needs to be assessed thoroughly, as widely available low cost and low technology abortion options could be crucial in meeting the Millennium Development Goal of decreasing maternal mortality by 75% by the year 2015.

Induced abortion is an intrinsic and inescapable element in the control of family size in all societies, whether the procedures are performed safely or unsafely.\textsuperscript{17} This study suggests that in a country where abortions have been performed unsafely, availability of misoprostol could reduce morbidity due to abortion. Prospective research will be needed to demonstrate causality between over-the-counter availability of misoprostol and a documented decline in abortion-related morbidity and mortality.

As suggested by this study, many women could benefit from more accurate information about the drug’s use, dosage and possible side effects. For example, both Gynuity Health Projects (www.gynuity.org) and Ipas (www.ipas.org) have Web sites where pharmacists and others can access proper doses, routes and side effects.

Further documentation of the potential positive impact of misoprostol on women’s health is imperative if it is to play a role in reducing abortion-related morbidity.

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References


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