Expectant, medical or surgical treatment for spontaneous abortion in first trimester of pregnancy: a cost analysis

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BACKGROUND: Misoprostol and expectant care have been shown to be acceptable alternatives to routine surgical evacuation for treatment of spontaneous abortion in the first trimester of pregnancy. The objective of this study was to analyse the cost of expectant care, misoprostol therapy and surgical evacuation. METHODS: A decision tree was designed to simulate the clinical outcome and health care resource utilization of surgical evacuation, misoprostol and expectant care for patients presenting with uncomplicated spontaneous abortion in the first trimester of pregnancy. Clinical inputs were estimated from literature and the cost analysis was conducted from the perspective of a public health care provider in Hong Kong. RESULTS: The base-case analysis showed that the misoprostol group (US$1000 per patient) was the least costly alternative, followed by the expectant care (US$1172 per patient) and surgical evacuation (US$2007 per patient). Rates of complete abortion using misoprostol and expectant care were identified as influential factors. Monte Carlo simulation (10,000 cohorts) showed that the misoprostol and the expectant care groups were less costly than the surgical evacuation group 100 and 88% of the time. The misoprostol group was less costly than the expectant group 100% of the time. CONCLUSIONS: Misoprostol therapy appears to be the least costly approach for treatment of uncomplicated spontaneous abortion.

Key words: cost analysis/expectant care/misoprostol/spontaneous abortion/surgical evacuation

Introduction

Spontaneous abortion occurs in 15–20% of all clinically recognized pregnancies (Laferla, 1986; Steer et al., 1989), mostly occurring in the first trimester of pregnancy. Surgical evacuation by dilatation and curettage (D&C) of the products of conception (POC) had been the most commonly performed standard treatment since the 1930s, even though complications such as uterine perforation, life-threatening haemorrhage or post-surgical pelvic infection may arise (Mackenzie and Bibby, 1978). In the past decade, expectant care and medical treatment have been shown to be effective alternatives for treatment of spontaneous abortion. A number of clinical trials reported that expectant management usually achieved complete evacuation of POC within 2 weeks of diagnosis with low infection rate (Nielsen and Hahlin, 1995; Luise et al., 2002). Misoprostol, a safe and inexpensive prostaglandin analogue, may provide prompt expulsion of POC when given alone and avoid complications associated with surgical evacuation and uncertainties of expectant treatment (Chung et al., 1995; Creinin et al., 1997).

The clinical effectiveness of various misoprostol regimens and expectant care have been examined in a number of trials, but it is difficult to compare the clinical outcomes with the published reports mainly due to the difference in diagnostic criteria of successful treatment and the duration allowed for complete abortion to occur before using surgical evacuation as salvage therapy. Beside clinical effectiveness, the cost associated with these treatment options is also a critical factor for health care providers and administrators to consider when selecting treatment approaches for spontaneous abortion, yet only a limited number of studies on the economic impact of the medical treatment have been reported (Hughes et al., 1996; Doyle et al., 2004; Graziosi et al., 2005). The objective of the present study was therefore to analyse the cost of expectant care, misoprostol therapy and surgical intervention for spontaneous abortion in the first trimester of pregnancy from the perspective of a public health organization in Hong Kong.

Materials and methods

Model design

A decision tree was designed to simulate, using probabilistic cohort simulation over a time-horizon of 2 weeks, the clinical outcome and health care resource utilization of three treatment approaches in a hypothetical cohort of patients presenting with signs and symptoms of uncomplicated spontaneous abortion in the first trimester of pregnancy: (i) surgical evacuation; (ii) misoprostol; and (iii) expectant care (Figure 1). In the arm of surgical evacuation, D&C was the only option offered to patients as it is the ‘gold standard’ management approach for spontaneous abortion in many regions. In the arms of misoprostol and expectant care, these two treatment options were offered as the alternatives to surgical evacuation for patients to select.
In the arm of surgical evacuation, patients would receive surgical evacuation of POC with 1 day of inpatient care and one follow-up in an outpatient clinic. Two possible clinical outcomes anticipated were: (i) complete abortion with no complication; and (ii) complication. Complications included the need for additional surgical evacuation, serious complications (e.g. uterine perforation, complication requiring hysterectomy, severe sepsis, organ failure), blood transfusion and localized pelvic infection (Nanda et al., 2005; Vazquez et al., 2005). Minor events with no or minimal medical resource consumption, such as use of analgesics, were not included.

In the arms of misoprostol and expectant care, those patients who did not accept these treatment options would undergo surgical evacuation. The patients who accepted the misoprostol or expectant care would be managed in the outpatient setting with two follow-up visits (ranged 1–3 clinic visits) within 2 weeks. Patients might have complete abortion with or without further need for surgical evacuation and would experience one of the four possible outcomes: (i) complete abortion with no complication; (ii) complete abortion with complications; (iii) need for surgical evacuation with no complication; or (iv) need for surgical evacuation with complications.

The total direct medical cost per patient was estimated for each treatment approach, including cost of primary treatment option for spontaneous abortion, cost of need for surgical evacuation when the primary treatment option failed, and cost of management of complications.

Clinical inputs
The rates of complete abortion and complications associated with study alternatives and patient acceptance rates for misoprostol and expectant care were estimated from clinical trials reported in the literature (Table I). A literature search on MEDLINE over the period of 1995–2005 was performed using key words ‘spontaneous abortion’, ‘surgical evacuation’, ‘misoprostol’ and ‘expectant care’. The selection criteria of clinical trials were: (i) reports written in the English language; (ii) trials included patients with miscarriage during the first 13 weeks of pregnancy with ultrasound evidence of retained POC or with clinical diagnosis of incomplete miscarriage; (iii) treatment outcomes assessed within 14 days; (iv) the number of patients requiring surgical intervention (or additional D&C if the primary treatment was surgical evacuation) and the incidence of complications (as listed above) were reported.

Data from a total of 29 reports were pooled. Eighteen studies were randomized clinical trials comparing misoprostol and expectant care with surgical management (one report) (Shelley et al., 2005), misoprostol versus surgical evacuation (six reports) (Chung et al., 1999; Demetroulis et al., 2001; Lee et al., 2001; Sahin et al., 2001; Muffley et al., 2002; Leung et al., 2004), expectant care versus surgical evacuation (three reports) (Nielsen and Hahl, 1995; Wieringa-de Waard et al., 2003, 2004), misoprostol versus expectant care (three reports) (Nielsen et al., 1999; Ngai et al., 2001; Bagratee et al., 2004) and various misoprostol regimens (five reports) (Creinin et al., 1997; Pang et al., 2001; Wood and Brain, 2002; Tang et al., 2003; Gilles et al., 2004). Nine reports were prospective cohort trials, including four studies on misoprostol treatment (Chung et al., 1995; Wagaarachchi et al., 2001; Coughlin et al., 2004), three studies on expectant care (Jurkovic et al., 1998; Luise et al., 2002; Blohm et al., 2003) and one study on expectant care and surgical evacuation (Chung et al., 1998) and one study on expectant care versus surgical evacuation according to patient preference (Wieringa-de Waard et al., 2002). One retrospective study on misoprostol treatment (Pandian et al., 2001) and one survey on patient acceptance of expectant care (Molnar et al., 2000) were also included. The misoprostol regimens used in the selected trials included daily dose of 400 mg to 1600 mg administered vaginally, orally or sublingually. The pooled averages of complete abortion and complications for each treatment option, and the patient acceptance rates of misoprostol treatment and expectant care were derived from the studies weighted against the number of patients in each study.

Cost inputs
The cost inputs of the model were estimated from the perspective of a public health organization in Hong Kong (Table I). The Hospital Authority is non-profit-making and the largest public health organization in Hong Kong. The services provided by the Hospital Authority are almost completely subsidized by the government. It charges patients who are non-residents of Hong Kong based upon the latest charges of health care services of public hospitals and clinics posted in the Hong Kong Gazette. Assuming that the charges listed in the Gazette represent only the cost components (including labour costs) with no addition of profits, the costs associated with each treatment outcome were therefore approximated using the charges as listed in the Gazette. The cost of complications was estimated from the percentage of serious complications (e.g. uterine perforation, complication requiring hysterectomy, severe sepsis, organ failure) and the need for additional surgical evacuation, and the percentage of less serious complications (e.g. blood transfusion and localized pelvic infection), associated with each treatment option, pooling from the literature. The cost of misoprostol was estimated by averaging the drug acquisition costs per Hospital Authority of the trial regimens in the studies.

Sensitivity analysis
Sensitivity analysis was performed by TreeAge Pro 2005 (TreeAge Software, Inc., Williamstown, MA, USA) and Microsoft Excel 2000 (Microsoft Corporation, Redmond, WA, USA) to examine the robustness of the model. All the parameters were examined over the high/low values or 95% confidence interval, if available. A univariate sensitivity analysis on all parameters was first conducted to screen for potentially influential factors. Selected two-way sensitivity analyses were further conducted on those variables with threshold values in the one-way sensitivity analysis. To evaluate the impact of the uncertainty in all of the variables simultaneously, a probabilistic sensitivity analysis was performed using Monte Carlo simulation. The cost of each study arm was recalculated 10000 times by randomly drawing each of the model inputs from a triangular probability distribution to determine the percentage of occasions in which each study arm would be the least costly strategy.
<table>
<thead>
<tr>
<th>Table 1. Clinical and economic inputs for the model</th>
<th>Base-case value</th>
<th>Range for sensitivity analysis</th>
<th>References</th>
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<tr>
<td><strong>Clinical inputs</strong></td>
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<tr>
<td>Rate of patient acceptance of expectant care (%)</td>
<td>64</td>
<td>62–66</td>
<td>Jurkovic et al., 1998; Molnar et al., 2000; Pandian et al., 2001; Luise et al., 2002; Wieringa-de Waard et al., 2002, 2004; Blohm et al., 2003</td>
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<tr>
<td>Rate of patient acceptance of misoprostol treatment (%)</td>
<td>86</td>
<td>83–89</td>
<td>Lee et al., 2001; Wagaarachchi et al., 2001; Tang et al., 2003</td>
</tr>
<tr>
<td>Rate of complete abortion using expectant care (%)</td>
<td>75</td>
<td>25–99</td>
<td>Nielsenn and Hahlin, 1995; Chung et al., 1998; Jurkovic et al., 1998; Nielsenn et al., 1999; Ngai et al., 2001; Luise et al., 2002; Wood and Brain, 2002; Wieringa-de Waard et al., 2003; Blohm et al., 2003; Bagrate et al., 2004; Shelley et al., 2005</td>
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<tr>
<td>Rate of complete abortion using misoprostol treatment (%)</td>
<td>69</td>
<td>50–95</td>
<td>Chung et al., 1995, 1997, 1999; Creinin et al., 1997; Pandian et al., 2001; Sahin et al., 2001; Demetroulis et al., 2001; Ngai et al., 2001; Pang et al., 2001; Muffley et al., 2002; Wood and Brain, 2002; Tang et al., 2003; Bagrate et al., 2004; Coughlin et al., 2004; Gilles et al., 2004; Shelley et al., 2005</td>
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<td>Rate of surgical complications (%)</td>
<td>6</td>
<td>0–11</td>
<td>Nielsenn and Hahlin, 1995; Chung et al., 1997, 1998, 1999; Sahin et al., 2001; Luise et al., 2002; Muffley et al., 2002; Leung et al., 2004; Shelley et al., 2005</td>
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<tr>
<td>Rate of treatment complications associated with expectant care (%)</td>
<td>1.7</td>
<td>0.7–2.6</td>
<td>Nielsenn and Hahlin, 1995; Chung et al., 1998; Jurkovic et al., 1998; Nielsenn et al., 1999; Ngai et al., 2001; Luise et al., 2002; Wood and Brain, 2002; Blohm et al., 2003; Wieringa-de Waard et al., 2003; Bagrate et al., 2004; Shelley et al., 2005</td>
</tr>
<tr>
<td>Rate of treatment complications associated with misoprostol treatment (%)</td>
<td>2.5</td>
<td>1.5–3.5</td>
<td>Chung et al., 1995, 1997, 1999; Creinin et al., 1997; Sahin et al., 2001; Demetroulis et al., 2001; Ngai et al., 2001; Pandian et al., 2001; Pang et al., 2001; Muffley et al., 2002; Wood and Brain, 2002; Tang et al., 2003; Bagrate et al., 2004; Coughlin et al., 2004; Gilles et al., 2004; Shelley et al., 2005</td>
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<tr>
<td>No. of outpatient clinic follow-ups for misoprostol treatment</td>
<td>2</td>
<td>1–3</td>
<td>Chung et al., 1995, 1997, 1999; Creinin et al., 1997; Demetroulis et al., 2001; Ngai et al., 2001; Pandian et al., 2001; Pang et al., 2001; Muffley et al., 2002; Wood and Brain, 2002; Tang et al., 2003; Bagrate et al., 2004; Coughlin et al., 2004; Gilles et al., 2004; Coughlin et al., 2004</td>
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<tr>
<td>No. of outpatient clinic follow-ups for expectant treatment</td>
<td>2</td>
<td>1–3</td>
<td>Nielsenn and Hahlin, 1995; Chung et al., 1998; Jurkovic et al., 1998; Nielsenn et al., 1999; Ngai et al., 2001; Luise et al., 2002; Wood and Brain, 2002; Blohm et al., 2003; Wieringa-de Waard et al., 2003; Bagrate et al., 2004</td>
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<tr>
<td><strong>Percentage of serious complications</strong> among patients who underwent:</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Surgical evacuation</td>
<td>50</td>
<td>–</td>
<td>Nielsenn and Hahlin, 1995; Chung et al., 1997, 1998, 1999; Sahin et al., 2001; Luise et al., 2002; Muffley et al., 2002; Leung et al., 2004</td>
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<td>Expectant care</td>
<td>27</td>
<td>–</td>
<td>Nielsenn and Hahlin, 1995; Chung et al., 1998; Jurkovic et al., 1998; Nielsenn et al., 1999; Ngai et al., 2001; Luise et al., 2002; Wood and Brain, 2002; Blohm et al., 2003; Wieringa-de Waard et al., 2003; Bagrate et al., 2004; Shelley et al., 2005</td>
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<tr>
<td>Misoprostol treatment</td>
<td>24</td>
<td>–</td>
<td>Chung et al., 1995, 1997, 1999; Creinin et al., 1997; Sahin et al., 2001; Demetroulis et al., 2001; Ngai et al., 2001; Pandian et al., 2001; Pang et al., 2001; Muffley et al., 2002; Wood and Brain, 2002; Tang et al., 2003; Bagrate et al., 2004; Coughlin et al., 2004; Gilles et al., 2004; Shelley et al., 2005</td>
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<tr>
<td><strong>Percentage of less serious complications</strong> among patients who underwent:</td>
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<td></td>
<td></td>
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<tr>
<td>Surgical evacuation</td>
<td>50</td>
<td>–</td>
<td>Nielsenn and Hahlin, 1995; Chung et al., 1997, 1998, 1999; Sahin et al., 2001; Luise et al., 2002; Muffley et al., 2002; Leung et al., 2004</td>
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<tr>
<td>Expectant care</td>
<td>73</td>
<td>–</td>
<td>Nielsenn and Hahlin, 1995; Chung et al., 1998; Jurkovic et al., 1998; Nielsenn et al., 1999; Ngai et al., 2001; Luise et al., 2002; Wood and Brain, 2002; Blohm et al., 2003; Wieringa-de Waard et al., 2003; Bagrate et al., 2004; Shelley et al., 2005</td>
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<tr>
<td>Misoprostol treatment</td>
<td>76</td>
<td>–</td>
<td>Chung et al., 1995, 1997, 1999; Creinin et al., 1997; Demetroulis et al., 2001; Ngai et al., 2001; Pandian et al., 2001; Pang et al., 2001; Muffley et al., 2002; Wood and Brain, 2002; Tang et al., 2003; Bagrate et al., 2004; Coughlin et al., 2004; Gilles et al., 2004; Shelley et al., 2005</td>
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<td><strong>Cost inputs (US$)</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient clinic (for misoprostol treatment and expectant care follow-ups)</td>
<td>90</td>
<td>72–108</td>
<td>–</td>
</tr>
<tr>
<td>Hospitalization per day</td>
<td>423</td>
<td>338–508</td>
<td>–</td>
</tr>
<tr>
<td>Dilatation and curettage</td>
<td>1308</td>
<td>1038–1577</td>
<td>–</td>
</tr>
<tr>
<td>Misoprostol treatment</td>
<td>1.5</td>
<td>0.5–2.3</td>
<td>–</td>
</tr>
<tr>
<td>Surgical complications</td>
<td>3192</td>
<td>500–5885</td>
<td>–</td>
</tr>
<tr>
<td>Treatment complications associated with expectant care</td>
<td>1577</td>
<td>500–5885</td>
<td>–</td>
</tr>
<tr>
<td>Treatment complications associated with misoprostol treatment</td>
<td>1900</td>
<td>500–5885</td>
<td>–</td>
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4E.g. uterine perforation, complication requiring hysterectomy, severe sepsis, organ failure.
5E.g. blood transfusion and localized pelvic infection.
Results
The base-case analysis showed that the misoprostol group (US$1000 per patient) was the least costly alternative, followed by expectant care (US$1172 per patient) and D&C (US$2007 per patient) (US$1 = HK$7.8). The one-way sensitivity analysis showed that the results of the model were sensitive to the variation of the rates of complete abortion using misoprostol treatment and expectant care. When the rate of complete abortion by misoprostol was <0.59 (Figure 2) or the rate of complete abortion by expectant care was >0.89 (Figure 3), the cost per patient in the misoprostol group would become higher than the expectant care group, whereas the cost per patient in the arm of surgical evacuation remained the highest throughout the ranges of all variables.

A two-way sensitivity analysis was further conducted with the rates of complete abortion using misoprostol treatment and expectant care (Figure 4) to examine their effects on the model. The combinations of variables on the line (threshold line) where the two zones met indicated that the misoprostol group and the expectant care group had the same cost per patient. The combinations of these two variables on the left side of the threshold line were associated with a lower cost in the misoprostol group, whereas the area on the right side of the threshold line indicated the combinations of variables leading to a lower cost in the expectant care group.

In the probabilistic sensitivity analysis, the results of 10 000 Monte Carlo simulations showed that the misoprostol and the expectant care groups were less costly than the arm of surgical evacuation 100 and 88% of the time, with mean cost-savings of US$1028 (95% CI 1025–1031) and US$286 (95% CI 282–290) per patient respectively. The misoprostol group was less costly than the expectant group 100% of the time by US$742 (95% CI 737–747) per patient.

Discussion
The results of our analysis showed that the direct medical cost per patient in the misoprostol group was the lowest among the three treatment approaches from the perspective of a public health organization in Hong Kong. The approach of using misoprostol therapy as an alternative to surgical evacuation would reduce 50% of the total direct medical cost per patient when compared with D&C as the only treatment choice. The misoprostol treatment approach was also less costly than expectant care by 15%. The probabilistic sensitivity analysis showed that these results remained the same 100% of the time in 10 000 cohorts.

The univariate sensitivity analysis showed that the direct medical cost of the surgical group remained the highest in all situations, while the cost of the misoprostol group became higher than the expectant care group when the rate of complete abortion using misoprostol treatment was <59% or when the rate of complete abortion using expectant care became >89%. Our findings showed that the need for surgical evacuation as salvage therapy, as indicated by the rate of complete abortion for misoprostol or expectant care, was the cost-driving factor. Similar findings were demonstrated in the few published studies on the economic aspects of medical treatment versus surgical evacuation in the management of spontaneous abortion. A cost-benefit analysis using decision analysis techniques to compare misoprostol and surgical evacuation had shown misoprostol to be the more cost-beneficial strategy (Doyle et al., 2004). Hughes et al. (1996) also reported a cost analysis based upon resource utilization in a randomized trial comparing medical versus surgical treatment. The base-case analysis of this study

![Figure 2. Change of cost per patient against the rate of complete abortion using misoprostol.](https://example.com/figure2)

![Figure 3. Change of cost per patient against the rate of complete abortion using expectant care.](https://example.com/figure3)

![Figure 4. Two-way sensitivity analysis on rate of complete abortion using expectant care and rate of complete abortion using misoprostol.](https://example.com/figure4)
showed that the direct medical cost per patient in the medical group was lower than the surgical group and the cost savings were a result of reduced utilization of the operating room. Similarly, another cost analysis on a randomized trial comparing misoprostol and surgical intervention also showed a lower direct cost per patient in the medical group, and the need for surgical intervention after medical treatment was also identified as the influential factor on the cost of treatment (Graziosi et al., 2005).

The two-way sensitivity analysis on the rates of complete abortion using misoprostol and expectant care identified the combinations of these two variables that were associated with a lower total cost in the misoprostol group and the expectant care group. If the rate of complete abortion using a misoprostol regimen was >50%, the complete abortion rate of expectant care was influential factor on the cost of treatment (Graziosi et al., 2005).

In conclusion, the present cost analysis shows that offering misoprostol therapy as an outpatient management alternative to surgical evacuation to patients presenting with uncomplicated spontaneous abortion appears to be the least costly treatment approach from the perspective of a Hong Kong public health organization. These considerations will become increasingly important in other health care systems struggling with often inadequate budgets. Spontaneous abortion is often the commonest indication for admission to hospital. Evidence from clinical trials increasingly shows, at least relative to a policy of universal surgical evacuation, both expectant and initial treatment with misoprostol are clinically acceptable alternatives.

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References


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