Introduction

Complications following abortion, be they spontaneous or induced, are a major threat to maternal morbidity and mortality particularly in the developing world. In such areas restrictive abortion laws and conservative cultural views have served only to cause a shift in balance of abortion procedures performed from those that are deemed safe and legal to those that are unsafe- the 'backstreet jobs'. WHO suggests that of the 43.8 million induced abortions performed in 2008, 21.6 million were classified as unsafe [(1)]. Of the 38 million induced abortions performed in less economically developed countries, 56% were also performed in an unsafe manner. Often following these procedures women will present later to a health care facility with an incomplete abortion as products of conception are retained or partially retained in the uterus. Those suffering from incomplete abortion may also be at substantial risk of infection, for instance, due to the high prevalence of human immunodeficiency virus in certain sub regions. Uterine perforation, septicaemia, haemorrhage and anaemia as a result of these "backstreet abortions" can also contribute to long term maternal morbidity as suggested by Weeks et al [(2)].

Readily available and easy access post abortion care is thus of great importance for the preservation of maternal health in low resource settings. In the past highly effective surgical interventions such as dilatation and cutterage, and more recently manual vacuum aspiration have been employed as the standard approach to treatment of incomplete abortions. Yet barriers to provision, such as lack of available resources and a dearth of facilities and trained providers, have called in to question how relevant surgical evacuation is in these low resource settings. Thus, the need for an alternative medical treatment has been highlighted.

Numerous studies have suggested that the prostaglandin E1 analog misoprostol may be a viable, safe and effective alternative treatment to surgical procedure, particularly to that of manual vacuum aspiration [(2-9)]. Its powerful uterotonic quality and ability to soften the cervix have, thus far, proved its potential in a wealth of other obstetric indications such as the induction of labour, use in post-partum haemorrhage and to induce abortion [(10)].These afore mentioned indications however are off-label uses of the drug, with misoprostol's licensed indication being for the prophylactic treatment of gastric ulcers. Thus as showcased in Figure 1[(11)] the

availability of misoprostol is somewhat limited, particularly in the low resource settings in which it could prove indispensable.

A 2005 study conducted by Weeks et al was one of the first to suggest the use of misoprostol for management of incomplete abortion in a low resourced hospital setting in Kampala, Uganda. An oral 600mcg dose of misoprostol was the treatment of choice. The drug was found to be easy to administer, reasonably priced and also, crucially in this instance, stable at ambient temperature. As well as proving successful

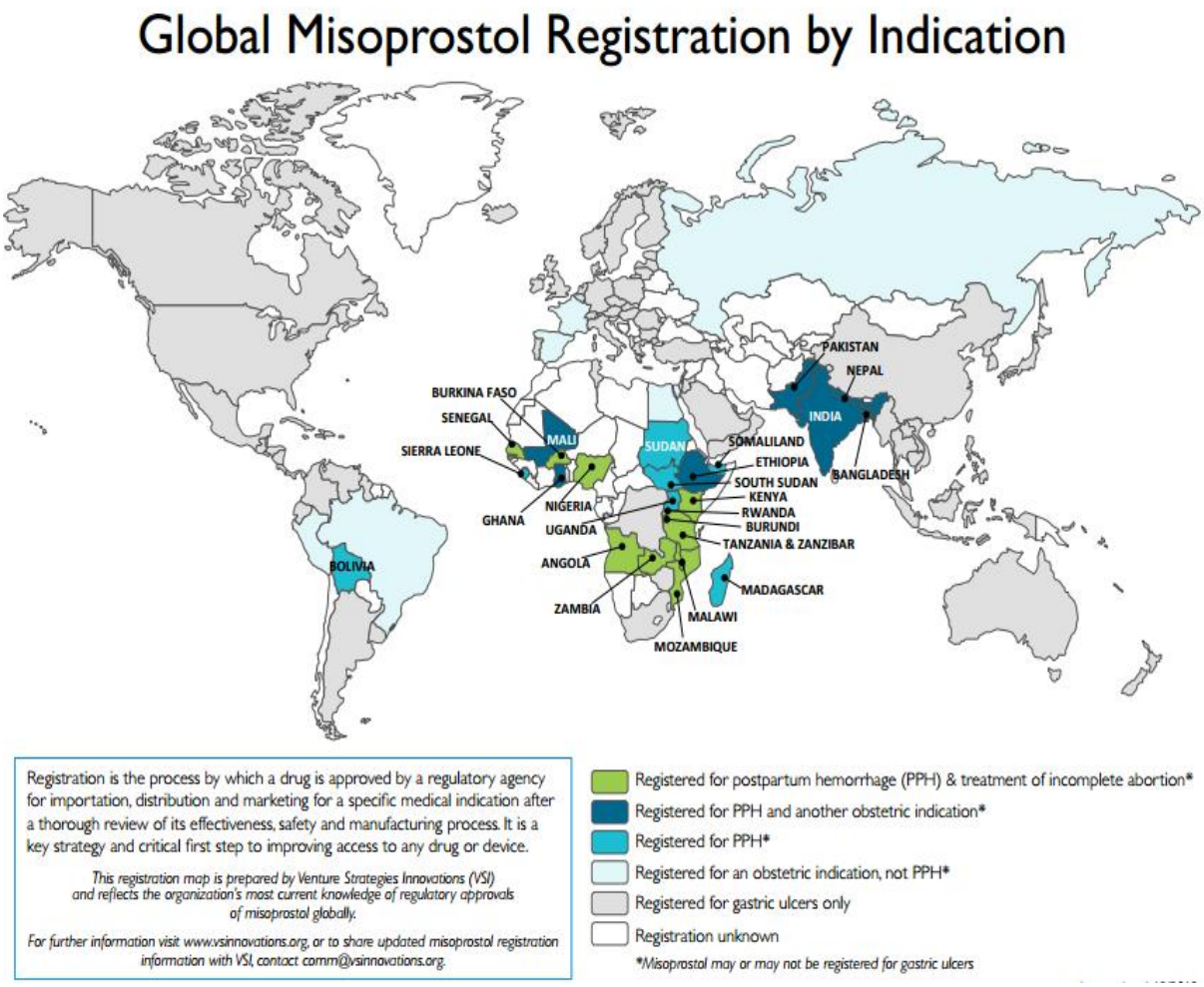

Figure 1[(11)] Countries where Misoprostol has formal drug registration(by indication)

successful in 96.3% of cases, there were a wealth of justifications for this medical management of incomplete abortion. Yet today, in 2014, misoprostol is still often not stated as the first line of treatment for incomplete abortion in many national health

Figure 1

guidelines, even with a place on WHO's list of essential medicines as of 2009 [12]. This review aims to explore once again the comparison of medical management of incomplete abortion with that of manual vacuum aspiration and to ascertain how certain measures, such as more comprehensive Post Abortion Care (PAC) and decentralization of its services, could contribute to a vast reduction in maternal mortality ratios.

Method:

For assessment of the use of misoprostol in comparison with manual vacuum aspiration, a literature review was chosen to evaluate the current research that was accessible. A multitude of studies were selected, in conjunction with numerous other resources from websites that were classed as relevant to the topic. When choosing which studies to include within the review, certain criteria were put in place when conducting the searches. Criteria to be fulfilled were, for instance, studies written solely in English and also that were published after the 2005 study by Weeks et al to allow for progression of ideas to be taken into account [2]. A search conducted including only those studies published before 2005 did not yield any results that directly compared misoprostol with manual vacuum aspiration.

An electronic search using the internet was led to source the studies with databases such as Scopus and Medline being the main tools used, as well, as the University of Liverpool's own database 'Discover'. Keywords that were used to refine the search included "misoprostol", "incomplete abortion" and "manual vacuum aspiration". The search conducted on Scopus including all three of the keywords yielded 19 results, 9 of which have been included in the review as they directly compared misoprostol and manual vacuum aspiration. The same keywords when entered into Discover yielded 101 results. A table showcasing the number of results achieved for each search can be found in the appendix of this review as Table 1. After reading the studies deemed relevant, any relevant references cited were also then searched for using their full title on Medline and then read to gain a broader insight into the topic. There are 8 studies in which misoprostol has been directly compared with manual vacuum aspiration as of 2005, these studies are thus the primary focus of this literature review.

Results:

In terms of successful evacuation of the uterus, both use of misoprostol and manual vacuum aspiration appear to be highly effective. The percentage of women reporting a fully completed abortion and thus not requiring further surgical intervention in the misoprostol groups of the studies ranged from between 91-99% in comparison to the MVA patients with values ranging between 99-100% [3-9]. In the 2005 study conducted by Weeks et al, MVA saw a greater degree of failure compared with 600mcg of misoprostol (91.5% versus 96.3%).In 2005 the suggested course of treatment for incomplete abortion was an oral dose of 600mcg of misoprostol [2]. A study conducted by Diop et al has since then alluded to the similarities in effectiveness between this method and a 400mcg sublingual alternative. The efficacy rates were 94.6% and 94.5%, for the oral and sublingual routes respectively [13]. Further comparisons between the 400mcg sublingual treatment and standard surgical evacuation have shown misoprostol to have a success rate of between 94.4 - 98.3 % and MVA between 99.7 - 100% [6,7]

Satisfaction ratings also appear high in the majority of cases for both methods. In all but one of the studies that had included a satisfaction questionnaire [6], MVA appeared to achieve greater support with findings of “satisfactory/ very satisfactory” ranging from between 94.7-108%. Misoprostol treatment deemed satisfactory/ very satisfactory” in the same studies produced results ranging from 94.2%-103%. [2, 3, 4, 5, 7, 8]. Although the differences are statistically significant in some cases, they are of little clinical importance.

Diagnostic technique

Diagnosis of degree of miscarriage can be determined by either bimanual examination in which an open external cervical os will discriminate between whether a miscarriage is threatened or not [14]. The use of ultrasonography prior to treatment will exclude threatened miscarriage and complete miscarriages, leaving those with true incomplete abortions to be treated, although parameters for incomplete diagnosis using sonography techniques are in themselves contested [16] As the reviews were conducted in less economically developed countries availability of ultrasound devices was restricted in all cases. Table 1 displaying its varying use can

be found in the appendix section of this review. The use of ultrasound to eliminate complete miscarriages prior to treatment is used less frequently in comparison to use post treatment to confirm expulsion of products of conception. Before treatment, three of the reviewed studies used no ultrasonography to determine the phasing of miscarriage [2,4,8]. In a number of studies there was inconsistency in ultrasonography use; it being used in varying amounts with hesitancy over the accuracy of clinical diagnosis being cited as the main reason to opt for this approach [5,6,7]. In the study conducted by Montesinos et al unrestrained ultrasound usage ensured inclusion of only those with an incomplete miscarriage in the trial [9]. Once treatment was completed, all but one study used ultrasound in varying degrees to assess successful outcomes [8]. The studies which did include ultrasound confirmation of completed abortion did so in differing amounts. Both Weeks et al and Shochet et al cited use in the case of persistent bleeding as well as presence of an enlarged uterus and also in the latter of the two studies, when ectopic pregnancy was suspected. More frequent usage of post treatment diagnostic sonography is also apparent in the misoprostol groups within the studies conducted by Montesinos et al and Shochet et al as well as within the private facilities included in the former study [6,9]. In only one study was there use in every case to confirm outcomes [3] , however, due to the constraints placed upon research in the Sengal site in the Shochet et al trial by a local ethics committee, mandatory use of ultrasound took place in this case as well[6].

Side Effects

In both the medical and surgical treatment of incomplete abortion, there appears to be a number of side effects that occur more regularly than others and at similar frequencies throughout the studies. Both pain/cramps as well as some form of vaginal bleeding appear to be the main adverse effects experienced in the selected studies. The degree of pain experienced was quantified using a Likert scale in a number of studies. Mean pain scores were given as values ranging between 2.63-3.00 in the misoprostol groups and 3.50-4.21 for MVA in two studies [4,8]. Whether or not the pain experienced was a reflection of first perceptions was alluded to by Dabash et al where 83.5% experienced less pain then expected with misoprostol in comparison to 43.9% with MVA [7]. Although this is the case, in a number of studies,

participants when prompted for a worst feature of their allocated treatment stated there was “none”. The percentage of participants treated with misoprostol who suggested this was in the range of 48.1%-75.2% and in the MVA group values were between 40.2%- 56.3%[2,5,9]. Tolerability of side effects also appears to be promising, with “easily tolerable/tolerable” provided as an answer in 77-95.5% of misoprostol cases and in 71%-100% of those having undergone MVA [3-8].Complications arising as a result of incomplete abortion in either of the two methods of evacuation were of a limited number. In the study by Weeks et al one woman treated with misoprostol and three women undergoing MVA contracted a pelvic infection [2]. Pelvic infection is also witnessed in misoprostol groups in the study by Dao et al and in a study comparing efficacy with misoprostol use in this indication between mid-level providers and physicians [3,16]. Occurrence of suspected and true ectopic pregnancies being misdiagnosed in women treated with misoprostol can also be seen in a number of studies [2,5,17]

Discussion

Participant Experience

Abortion is a traumatic experience for many women, regardless of whether treatment is provided in tablet form or surgically. The less invasive nature of misoprostol has the potential to address anxieties or wishes to avoid surgical intervention [7,9] with 12% of women in the study conducted by Dao et el citing the best feature of the drug as it being “less traumatic” [3]. Yet although misoprostol is stated as being a “simple quick an successful method” by 37.9% of women in the Dao et el study, in other trials MVA had a greater percentage of women describing it as quick and simple method [2,5,7,8]. This is perhaps an outcome that reflects what Osur et al suggests as women’s comfort in the knowledge of completion before leaving a facility [18]. Less prolonged bleeding after treatment [4,5,7,9] and the appreciation of seeing the products of conception expelled [7,9] with MVA gives the procedure a sense of finality for women at an earlier stage than misoprostol.

Numerous studies experienced problems with the loss of women to follow up [2,5,6,8] . In the women who did not return for follow up meetings it could be inferred that successful outcomes may have potentially occurred and thus the need for further contact with the health care facility was diminished, as those women who did

experience complications sought professional help [2,5]. In those receiving MVA, Weeks et al suggests that the discomfort experienced during treatment and the stigma attached to abortion in some cultures may have acted as a deterrent for follow up return [2]. As mentioned previously unwillingness to return when complications are not encountered may also be a result of a cultural belief in only seeking healthcare in the case of emergency [8].

Financial Costs

In low resource settings cost will always be a major precipitating factor in the viability of a treatment option. The burden placed upon health care services by surgical procedure is of large proportions. The lack of trained providers, equipment and facilities required to provide MVA as the first line for treatment for incomplete abortion highlights the need for an alternative treatment [17,19]. Misoprostol offers a cheaper alternative to MVA, not only its 600mcg oral route but also administered at 400mcg sublingually as suggested by Diop et al [13] and confirmed by numerous other studies [17,19,20,21]It should also be noted that conservative management of incomplete abortion is also a viable option that also avoids costly surgical intervention and in a study conducted by Luise et al appears to be the preferred treatment method[22].

Variability in Study Conditions

Due to a lack of country based standards and routine protocol the studies reviewed showcase a wide variety in setting and management. The primary example of this is seen in the use of ultrasonography. Studies achieving greater success were those that did not use or had limited use of ultrasound to exclude complete miscarriages prior to treatment [4,5,7]. Studies in which ultrasound was used liberally to confirm abortion status after treatment witnessed a lower degree of efficacy particularly notable in the studies conducted by Dao et al , in the private facilities included by Montesinos et al and in the Sengal site of the Shochet et al study [3,6,9]. It seems ultrasound should thus be used with a degree of trepidation, not only due to its cost, but also due to its increased sensitivity over clinical examination, removing the threat of misdiagnosis of incomplete abortion at follow up and the incidence of higher rates of success when inevitable and complete miscarriages are included in patient groups.

Differences in healthcare settings between the reviewed studies as well as within the studies themselves also have a bearing on results. Study conditions at tertiary level healthcare facilities are much harder to replicate at a lower level as noted by the only study conducted in such a manner [6], where ultrasound was not used before or after treatment. With no women lost to follow up in the Shwekerela et al study it seems that at low level settings women are not as transient as perhaps they are at higher levels and access to transportation to facilities is less of a barrier to the more rural community. The thorough nature of the post abortion care showcased within certain studies, although comprehensive, is not easily replicable in day to day life as suggested by Taylor et al and Dao et al [3,5]. Scheduled appointment follow up and comprehensive counselling sessions does not only require large quantities of time but also contributes to financial burdens of low level facilities in particular. Further studies of the comparison of misoprostol and MVA at lower level facilities would thus add further evidence for the need for decentralization of healthcare in less economically developed countries and provide a more accurate representation of daily clinical experiences.

Treatment providers

The experience required of those providing the treatment with misoprostol appears to also add to its potential as an alternative treatment for incomplete abortion. A number of the studies were thus nurse-led, demonstrating the ability of mid-level providers in this instance [2,5,8]. The benefits of such task-shifting could be numerous with a decrease in time constraints placed upon physicians and cost reduction. Yet in some cases a lack of experience with new techniques can lead to a decrease in successful outcomes as witnessed in the trial by Shochet et al; this would suggest a greater emphasis is to be placed upon comprehensive provider training in future [6]. Concerns over implementation of new treatments it appears may have lead, in some instances, to a degree of provider bias as suggested by Dao et al [3]. Over interpretation of ultrasound scans [3] and greater prompting of patients at the recall of misoprostol related side effects [8] are suggested examples of this.

Education

It seems a key issue in the ability to treat incomplete abortion lies in the education of the women affected. One target point associated with misoprostol is it not possessing a licence for obstetric indications and thus it being sold as 200mcg

tablets without vital package information. Without crucial knowledge provided by guidelines about the wide variety of dosages for different indications accidental misuse with self-administration could occur [23]. As previously suggested it does not seem feasible in such settings to provide follow up appointments after misoprostol treatment. Education of women to recognise the symptoms of the retention of products of conception would thus remove the need for this[9]. Further study in to what form of follow up care could prove a viable alternative could be key in the development of post abortion care services. It seems the inclusion of comprehensive family planning advice into the care plan for those presenting with incomplete abortion would also lessen demands placed upon abortion services [7,20]. Often women seeking treatment have had previous abortions, with greater emphasis placed on how to avoid pregnancy originally there could be a reduction in cases of incomplete abortions.

Conclusion

In conclusion, the reviewed literature suggests that the levels of safety and efficacy of misoprostol treatment for incomplete abortion make it a viable alternative for manual vacuum aspiration in low resource settings. As is the case with the many health issues facing developing countries, financing is at the epicentre of the majority of healthcare decisions. Misoprostol is not only cost-effective but also yields high levels of efficacy as showcased by numerous trials. This simple medical treatment could greatly reduce pressures placed upon already over-burdened facilities, with its simplicity allowing low level facilities to establish themselves as providers of comprehensive post abortion care. The use of misoprostol as first line treatment could ensure entitlement to sexual and reproductive health and rights, including access to safe incomplete abortion resolution, would not be based upon financial standing.

Since the 2005 study conducted by Weeks et al [2] was published misoprostol has been included on WHO's list of essential medicines with regards to incomplete abortion, yet it is still classed as off-label usage for this indication [12]. The lack of licence and many countries unwillingness to include the drug on national essential medicine lists is only further burdening national healthcare systems and resulting in under stocking of a drug which could be hugely beneficial to large numbers of

women. The wealth of literature addressing the successes of misoprostol is suggestive that it is not further scientific trials that are needed but urgent intervention by those in charge of health care systems in these countries. Hence forth, it would be erroneous and unacceptable for Non-Governmental Organisations and Ministries of Health to further neglect the incorporation of misoprostol as first line treatment for incomplete abortion, especially for the women of developing nations.

Appendix

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Key words searched	Number of result: Scopus	Number of results: Discover
'Misoprostol'	3886	9,556
'Manual Vacuum Aspiration'	136	687
'Incomplete Abortion'	499	173
'Misoprostol' + 'Manual Vacuum Aspiration'	51	237
'Misoprostol' + 'Incomplete abortion'	182	477
'Incomplete abortion' +'Manual Vacuum Aspiration'	39	183
'Misoprostol' + 'Incomplete abortion' +'Manual Vacuum Aspiration'	19	101

Table 1: Results from Online Database Searches

Study	Country	Facility Setting & number of participants (n)	Use of ultrasound before treatment?	Excluded complete miscarriage?	Ultrasound confirmation of complete abortion post treatment?	Time of Primary outcome	Misoprostol Success Rate	MVA Success Rate
Weeks et al	Uganda	Tertiary level (n=312)	No	No	Yes (only with persistent bleeding/ enlarged uterus)	Between 7 & 14 days	96.3%	91.5%
Shwekerela et al	Tanzania	Low- level (n=300)	No	No	Yes (used in 3 cases in misoprostol group)	Day 7	99%	100%
Dao et al	Burkina Faso	University teaching hospitals (n=442)	Yes	Yes	Yes	Day 7	94.5%	99.1%
Bique et al	Mozambique	Tertiary level (n=270)	No	No	No	Day 7	91%	100%
Dabash et al	Egypt	Tertiary level (n=695)	Yes/No (1/3 of cases)	Yes/No (1/3 of cases)	Yes (used in 1/5 of cases)	Day 7	98.3%	99.7%
Taylor et al	Ghana	Tertiary level (n=218)	Yes (if unsure	Yes/No	Yes/No	Day 7	98.1%	99.1%
Montesinos et al	Ecuador	2 sites: Public tertiary Private Secondary (n= 203)	Yes (both sites)	Yes (both sites)	**Private:** 95.5%- misoprostol 21.1%- MVA **Public**: 28.6%-Misoprostol 17.9%- MVA	Day 7	**Public**:96.4% **Private**:86.4% Average:94.3%	100%
Shochet et al	5 sites (Senegal, Niger, Mauritania, Nigeria and Burkina Faso)	Varying (n=839)	Yes/No	Yes/No	Yes (only with persistent bleeding/ enlarged uterus or suspected ectopic pregnancy) Senegal: used in over 81% Other 4 sites used in: - misoprostol group: 27.1% -MVA group: 17.5%	Day 7	91.8% (Range between sites: 88.7%-97.6%)	99.4%

Table 2: Use of Ultrasound in Various Studies