WHO/RHR/HRP/08.06

UNDP/UNFPA/WHO/WORLD BANK
Special Programme of Research, Development and
Research Training in Human Reproduction (HRP)

Impact of HRP research in medical (non-surgical) induced abortion: a case-study

Reviewer

Jane Norman
Regius Professor of Obstetrics and Gynaecology,
University of Glasgow, Glasgow, Scotland

With assistance from

William Winfrey
Futures Institute, Glastonbury, CT, USA
for the economic analysis

UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP). External evaluation 2003–2007; Impact of HRP research in medical (non-surgical) induced abortion: a case-study.

Printed in Switzerland

Contents

Executive summary

Unsafe abortion, defined as "a procedure for terminating an unintended pregnancy carried out either by persons lacking the necessary skills or in an environment that does not conform to minimal standards, or both", remains a major public health problem. Medical abortion, that is abortion effected by drugs rather than a surgical procedure, is a safe and effective alternative to surgical abortion and can potentially play a major role in reducing unsafe abortion.

Methods

This review was conducted on the basis of face-to-face meetings with HRP personnel and other stakeholders and by a review of the published literature on medical abortion from WHO and other sources. The focus of the review was activities between 1997 and 2007.

Findings

HRP's work on preventing unsafe abortion included highlighting the issue; conducting, analysing and publishing clinical trials on medical abortion; preparing guidelines; and collaborating on promoting the use of Medabon®. HRP's direct expenditure on research on medical abortion was US$ 1.7 million over the eight-year period 1999–2007.

The outputs fall into three categories: an extensive, widely cited list of original publications; registration of Medabon®; and addition of mifepristone and misoprostol to the *WHO model list of essential medicines*. Other outputs include contributions to meta-analyses and systematic reviews, organization of sessions at conferences, conduct of local and regional workshops, generation of new research questions, and individual and institutional capacity-building.

HRP worked with 15 medical centres and three academic institutions in conducting its clinical trials and in public–private partnership with the (not-for-profit) Concept Foundation and the pharmaceutical firm Sun Pharma in the registration and production of Medabon®.

Cost–effectiveness (including finances)

The price of Medabon® is significantly lower than both the public and private sector prices of its components, mifepristone and misoprostol. Estimation of the numbers of women worldwide who could access Medabon® at its anticipated cost, but who could not afford mifepristone marketed by current manufacturers and who would otherwise choose unsafe (surgical) abortion, indicates that 1 million unsafe abortions and 3600 maternal deaths could be averted annually by registration of Medabon® where abortion is legal. HRP expenditure on medical abortion over the past eight years could be translated into a projected cost of US$ 0.95 per unsafe abortion averted and US$ 264 per maternal death averted.

Outcomes and global public goods

Most of HRP's work in medical abortion during the decade (1997–2007) involved conducting clinical trials. Five of the seven large randomized clinical trials conducted in developing countries in the past 10 years were undertaken by HRP. These trials are of the highest quality, have clear relevance for clinical service provision and were conducted with sufficient rigour and detail that they can be used to support licensing applications for mifepristone and misoprostol. This is unusual for academic clinical trials, and HRP deserves to be congratulated for having achieved this degree of quality. HRP-run clinical trials have been cited (which is a quality indicator) twice as often as the two large trials conducted by other organizations in developing countries during this period.

Additionally, HRP has disseminated the results of these trials in evidence-based clinical guidelines and reports. They have also, in strategic reviews of abortion provision generally, helped governments to develop strategies for introducing medical abortion.

HRP also collaborated with the Concept Foundation to enable the manufacture, registration and distribution of a low-cost, good-clinical-practice standard medical abortion product (Medabon®) to the public sector in developing countries. This ambitious and novel approach has enabled translation of HRP clinical research into a formulation that can benefit developing countries.

Impact

HRP's work has contributed to changing the global health status, with a demonstrated 5.4% reduction in maternal mortality between 1990 and 2005, and work on preventing unsafe abortion is likely to effect further reductions. The rate of unsafe abortions per 1000 women of reproductive age has also declined.

There has been a significant increase in access to medical abortion: Medabon® is now registered in one country, and registration is pending in a further 10 countries. The work of HRP on misoprostol allows health-care providers to recommend a safe regimen (albeit less effective than the mifepristone–misoprostol combination) in countries where mifepristone is unavailable. Where medical abortion with mifepristone is legally available, about 50% of women chose this option for inducing abortion.

Conclusions

Successes and failures

The major success of HRP's work in this area is the good clinical practice standard clinical trials, which have provided an important knowledge base for medical abortion practice and enabled registration of a low-cost formulation. The strengths of these trials include collaboration between HRP and research centres and individuals, which allowed these trials to be completed as planned within a small budget. The work done by HRP during the period is highly cost–effective and is likely to have a major impact in reducing unsafe abortion.

There are no apparent failures or major weaknesses of HRP's work in this area. Funding shortfalls have necessarily limited the scope of activity.

Lessons learnt

Timely publication is crucial in translating HRP's work into practice. The excellent data from the clinical trials must now be matched by research on how to introduce Medabon® into countries where abortion is legal.

Recommendations

- HRP should sustain its influential, evidence-based, highly respected leadership in facilitating safe medical abortion, replacing unsafe practices.
- WHO, other cosponsors and members of the Policy and Coordination Committee should help the new Director of HRP to maintain HRP's work in prevention of unsafe abortion.
- Now that much of the work has been done to define an appropriate regimen, future work should focus on barriers to service delivery and on synthesis of evidence.
- The WHO management hierarchy should review its internal procedures for approving publication of work on abortion, including medical abortion, and set targets to minimize the delays.

Introduction

HRP has been active in the field of medical abortion since the early 1980s. The most recent review of HRP's activities in this area was performed in 2003, when Management Sciences for Health and the Swiss Centre for International Health jointly reviewed HRP's programme. The present review was commissioned in 2007, with the aim of evaluating how, by investing in HRP, the world has changed in terms of medical abortion.

Methods

- Meetings with personnel in HRP (Helena von Hertzen, Peter Fajans, Ronald Johnson, Iqbal Shah, Craig Lissner and Jane Cottingham) to map the scope of HRP's activities (especially clinical trials, interaction with governments, nongovernmental organizations, commercial companies, patient groups and advocacy).
- A literature search in Medline to identify published clinical trials; assessments made of quality, impact (including impact factor) and contribution to knowledge generally.
- Review of HRP's web site to determine other activities related to medical abortion (e.g. publications, guidelines, policy initiatives and activities mentioned in newsletters).
- Review of a synthesis of the evidence on medical abortion from the *WHO Reproductive Health Library*.
- Internet search on Google to identify other references.
- Information from HRP personnel on unpublished activities, e.g. presentations at conferences, training workshops, interactions with governments and nongovernmental organizations, and advocacy.
- Review of trends in use of medical abortion worldwide (where possible), abortion-related deaths, access to medical abortion and access to abortion itself during the period under study.
- Review of other articles on medical abortion (review articles and editorials) for background information against which HRP's work was conducted and to determine the impact of HRP's activity.
- Review of web sites and publications of other groups in this area [e.g. Gynuity Health Projects, William and Flora Hewlett Foundation (www.id21.org), the postabortion care consortium (www.pac-consortium.org), Guttmacher Institute] to establish their activities and elicit comments on HRP's activity in medical abortion during this period.
- Interviews with other players: Khama Rogo, Beverly Winikoff and Peter Hall.
- Teleconferences with Douglas Huber and William Winfrey.

Rationale

Unsafe abortion, defined by WHO (WHO, 1992) as “a procedure for terminating an unintended pregnancy carried out either by persons lacking the necessary skills or in an environment that does not conform to minimal standards, or both”, remains a major public health problem. It is estimated that in developing countries, one woman dies every eight minutes due to the complications of an unsafe abortion, and the procedure accounts for around 13% of maternal deaths (WHO, 2007a). Detailed modelling of abortion-related maternal deaths suggests that medical methods might have a major impact in reducing mortality related to unsafe abortion, especially in developing countries (Harper et al., 2007).

The stated aims and responsibilities of WHO are to provide leadership on global health matters, shape the health research agenda, set norms and standards, articulate evidence-based policy options, provide technical support to countries and monitor and assess health trends. Provision of medical abortion (where abortion is legal), to prevent unsafe abortion, is entirely consistent with these aims and is mandated by paragraph 8.25 of the Programme of Action of the International Conference on Population and Development (ICPD, Cairo, 1994) (Annex 1). The mandate was reinforced in 1999 at the five-year review of the ICPD Programme of Action by the

- find safe alternative approaches to pregnancy termination; and
- formulate evidence-based technical and policy guidance on safe abortion.

The comparative advantage of HRP over other groups in its work in medical abortion was outlined in some detail during the previous review. The breadth, capacity, prestige and credibility of HRP, with its international composition and links with national governments, was highlighted, and its international leadership in the area of unsafe abortion was emphasized (External Evaluation 1990–2002, available at www.who.int/reproductive-health/management/index_hrp.html).

Unsafe abortion, like many health problems, disproportionately affects women in low-income and developing countries. The incidence is eight times higher than in developed countries (16 compared with two per 1000 women of reproductive age), with the highest rates in least-developed countries (25 per 1000 women of reproductive age) (WHO, 2007). One thousand-fold more deaths occur in developing countries than in developed countries due to unsafe abortion.

Global public goods were defined by the Independent Evaluation Group of the World Bank