Cervical cancer in developing countries: how can we reduce the burden? Awareness raising, screening, treatment and palliation

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Trop Doct 2007 37: 67

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>> Version of Record - Apr 1, 2007

What is This?
Cervical cancer in developing countries: how can we reduce the burden?
Awareness raising, screening, treatment and palliation

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TROPICAL DOCTOR 2007; 37: 67–70

SUMMARY  Cervical cancer is an important health problem in developing countries. Most women present with advanced disease, resulting in low cure rates. Screening by Visual Inspection with the Aid of Acetic Acid and optionally HPV DNA detection as a second test is technically feasible. However, the majority of women appear to be reluctant to attend a screening clinic. This is probably due to lack of knowledge and a low priority of women’s health in local communities. There is an obvious need to obtain more knowledge on communities’ perceptions and understanding of cervical cancer. Furthermore, we need more information on what issues should be addressed in order to perform cervical cancer screening in an acceptable manner.

Treatment of cervical cancer in developing countries is highly dependent on the resources and skills available.
Efforts to provide adequate palliation should be enhanced as relief of troublesome symptoms can often be achieved by relatively simple and low-cost measures.

Introduction
Cervical cancer is an important health problem in developing countries that can be reduced by simple and low-cost tools. In this review, possible strategies to reduce the burden of this lethal but preventable disease will be discussed.

Epidemiology
The worldwide annual incidence of cervical cancer is an estimated 470,000. At least 80% of cervical cancer cases occur in developing countries. Nearly 200,000 women in developing countries die of this disease each year. In the majority of underprivileged countries, it is the most common cancer in women. Approximately 75% of cervical cancer cases in developing countries are diagnosed in advanced stages that are difficult to cure.1,2

Aetiology and risk factors
It is now well established that a genital infection with one of the oncogenic types of human papillomavirus (HPV) is the most important aetiological factor for cervical cancer. Other biological factors that contribute to the development of cervical cancer are early first intercourse, a promiscuous male partner, human immunodeficiency virus (HIV) infection and smoking.1,3 Among the sociocultural factors that contribute to the development and high incidence of cervical cancer are lack of education and awareness, and low priority of women’s health.
Synergy of several of these risk factors may result in the development of cervical intraepithelial neoplasia (CIN). In women with unfavourable characteristics, such as oncogenic type HPV and impaired immunity, CIN may progress to cervical cancer.
Since 1993, cervical cancer has been considered to be an ‘AIDS-defining’ condition. This implies that if an HIV-positive woman develops cervical cancer, she is deemed to have AIDS. However, whether HIV increases the risk of cervical cancer remains to be established.
There are suggestions that HIV has an independent effect on the development of CIN. This finding should be interpreted with caution as most women with an HIV infection are very often also infected by HPV, with a consequently high risk of CIN. Careful adjustment for such confounding suggests that there is an independent but small effect of HIV on risk of CIN.4

Prevention of cervical cancer by vaccination?
Recently, several placebo-controlled randomized controlled trials on vaccination against oncogenic HPV types were published and summarized in the British Medical Journal.5 The results of the vaccination studies are encouraging as it was shown that the incidence of HPV 16 and 18 infections was lower in the group that was treated with the vaccine in comparison to the placebo group. In addition, less pre-invasive lesions of the cervix were seen.6,7
However, it remains to be proven that an HPV vaccine will protect against cervical cancer. Several questions are still to be answered, such as:
• How long will the vaccine protect?
• What level of antibodies is needed to result in an effective protection?
• At what age should vaccination start?
• Should men be vaccinated?
• Do the currently applied vaccines protect against all oncogenic HPV types?8
Until these and many more questions are addressed, screening will be an important tool to reduce the burden of cervical cancer.
Screening

Rationale

Unlike many cancers, cervical cancer is a preventable disease, but it is lethal if not treated. Relatively inexpensive screening techniques can reduce the burden of cervical cancer by detecting the disease in a pre-invasive or early stage. Pre-invasive lesions can easily be treated and cured. The same goes for the majority of women with early-stage cervical cancer. Unfortunately, there is a lack of effective screening programmes for cervix cancer in most developing countries. This is one of the reasons for the high incidence of cervical cancer in developing countries.

Setting a target population

Screening should be population based and accessible at low cost. Preferably, it is offered in combination with other reproductive health issues. It is essential to discuss the importance of the screening with local authorities in order to achieve as wide acceptability as possible within the community.

The screening programme should be population based, i.e. targeted on all women (realistically >80%) within a specified age group. Due to the long course of development from pre-invasive disease to frank invasive cancer, a once in a lifetime screening for all will result in the detection of more (pre)invasive lesions than using the test repeatedly on a smaller number of women.

Based on the known peak incidence for pre-invasive and invasive diseases, all women should be offered at least one cervical screening test in their lifetime at approximately 40 years of age. When resources are available, the screening programme could be extended to 10 yearly screening tests at 35,45 and 55 years of age, provided that 80% coverage can be reached.

It is advisable to perform the screening at the primary health centres closest to the target population. Existing grassroots level health workers can be deployed to identify eligible women within a defined area and to bring them for screening to the health centres. There the tests can be administered by a trained nurse, auxiliary nurse midwife or health worker.

Which test? Potentials and limitations of screening tests

Screening tests are tools to identify those women in whom further investigations are needed in order to establish or rule out the diagnosis of a (pre)invasive cervix lesion, i.e. CIN or cancer. Unfortunately, there is a widespread misunderstanding regarding the significance of a positive screening test. A positive test result, whether it is a pap smear or any other test, may reflect a suspicion of cancer. The definitive diagnosis can only be established through histological examination of a tissue biopsy. It is of paramount importance that all health-care workers involved in the care for women with gynaecological problems have a good understanding of the possibilities and limitations of cervical cancer screening tests.

What screening technique should be applied? For several reasons, pap smear screening as the primary screening tool is not appropriate in most developing countries. Pap smear screening requires a complex organization and infrastructure, skilled smear takers, well-organized administrative infrastructure and support, a sufficient number of cytotechnologists and pathologists, laboratory facilities and an effective follow-up system. These facilities are often lacking.

Fortunately, however, it has become well established that a more simple screening technique, Visual Inspection with the Aid of Acetic Acid (VIA), approaches the effectiveness of pap smear screening. Although specificity is somewhat lower, sensitivity of VIA approaches that of pap smear. Of all cervical cancers, 70-85% are detected with this simple and low-cost test.

VIA can be performed by nurses and midwives who have been trained in a 2-3 course. The cervix is inspected with the naked eye before and after application of acetic acid. Women with an abnormal VIA result should be referred for colposcopy and biopsies should be taken, if needed. By histological examination of these biopsies, a diagnosis can be established and treatment provided, if indicated. This screening policy has proven its effectiveness in a large randomized study conducted in India.

Instead of immediate referral of all women with an abnormal VIA result, HPV DNA detection may be added as a second test at the same visit. Blumenthal has shown that the specificity of the screening procedure improves considerably by adding a second test.

However, HPV DNA detection tests are relatively costly. Another disadvantage is the delay in availability of the test result. Hence, making management decisions based on VIA alone is often the most realistic option in settings where there is a considerable loss to follow-up.

Acceptability and community perceptions

A recent study from Thailand on the feasibility and acceptability of screening programmes has shown that, for those women who participate, screening is acceptable. However, even after intensive information campaigns, only 17% of eligible women were actually screened. In a recent Indian study, a higher participation rate (63%) was reported. This is probably due to a very personal approach of the target population, as all eligible women were visited at home by a female health worker who explained the nature of the study.

It is not entirely clear why women are reluctant to undergo screening for cervical cancer. Several studies among women living in developing countries have revealed that knowledge about cervical cancer is limited. Another factor that may be of importance is the knowledge and attitude of men towards screening or treatment of gynaecological morbidity. Men often have very influential roles in the decision-making process of whether to seek health care for reproductive tract illnesses.

Thus, it has been established that screening for cervical neoplasia is feasible when considering technical and logistic aspects. However, even in a high-profile research setting, the majority of target populations are not reached, probably due to acceptability problems.

Hence, further research examining community perceptions and understanding of gynaecological morbidity, in particular cervical cancer, is warranted. If interventions to improve health are truly to benefit women, they must be developed from the start with a critical understanding of women’s own perceptions of their health problems and needs.
Currently, a study on these issues using qualitative instruments\textsuperscript{20} is being conducted in Bangladesh. It is expected ... IVA Invasion into bladder and/or rectum
Stage IVB Distant metastases

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Standard treatment is simple hysterectomy. Conization is
the frame of a screening programme. For stage IA1
inspections should be best conducted.

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will, to a great extent, depend on the resources and skills
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curative treatment for cervical cancer is not realistic. This
is due to late diagnosis as well as to lack of resources.
However, health-care providers can still help these women
by trying to control their symptoms.

Cancer pain is often grossly under-treated. This issue is of
concern because more than 80% of patients with cancer pain
find adequate relief through the use of simple drugs.\textsuperscript{27} It
is advisable to start with paracetamol up to 3 g a day in three
to six doses. If this is not sufficient, an NSAID (non-steroidal
anti-inflammatory drug) should be added. The third step
encompasses opioids. Opioids are inexpensive and effective.
They should be administered every 4–6 h, but slow release
morphine is administered 2–3 times daily. If the dose is too
low, it should be increased by 50%. It is essential to add a

Table 1 FIGO staging (1995) for cervical cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA1</td>
<td>Tumour limited to cervix, invasion max. 3 mm, width max. 7 mm</td>
</tr>
<tr>
<td>IA2</td>
<td>Tumour limited to cervix, invasion 3–5 mm, width max. 7 mm</td>
</tr>
<tr>
<td>IB</td>
<td>All larger tumours that are limited to the cervix</td>
</tr>
<tr>
<td>IIA</td>
<td>Tumour with extension to upper two thirds of vagina</td>
</tr>
<tr>
<td>IIB</td>
<td>Tumour with extension to parametria, pelvic side wall is not involved</td>
</tr>
<tr>
<td>IIIA</td>
<td>Tumour with extension into lower one third of vagina</td>
</tr>
<tr>
<td>IIIB</td>
<td>Tumour extended to pelvic side wall uni- or bilateral and/or hydrenephrosis</td>
</tr>
<tr>
<td>IVA</td>
<td>Invasion into bladder and/or rectum</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>

Pre-invasive lesions and early invasive cervical cancer are usually asymptomatic, and these will only be detected by screening.

Symptoms of cervical cancer are: postcoitum bleeding, irregular bleeding and vaginal discharge in the early stages. In case of advanced disease, additional symptoms like voiding problems and lower back pain, pain in one leg, lymphedema, weight loss and ureaemia may occur.

On physical examination, an exo- or ulcerating tumour origininating from the cervix is seen. The tumour may be limited to the cervix, but will usually grow laterally into the parametria or distal into the vagina.

Diagnosis is established by histological examination of a tissue biopsy. This can be taken in an outpatient clinic without an anaesthetic.

For cervical cancer, as for all gynaecological cancers, the international federation of obstetrics and gynaecology (FIGO) staging system is used (see Table 1). Cervical cancer spreads mainly lymphogenic, first to the pelvic nodes, and later to the para-aortic nodes.

Treatment of pre-invasive lesions

Most pre-invasive lesions can be treated effectively by cryocoagulation, large loop excision of the transformation zone (LLETZ) or conization. However, follow-up after local treatment is warranted. It is anticipated that this is not feasible, and if there is no further pregnancy wish, hysterectomy is a good definitive treatment.

Treatment of invasive cancer

In developing countries, management of cervical cancer will, to a great extent, depend on the resources and skills available. Hence, standard treatment as described in a textbook\textsuperscript{21} is often not feasible. Possible options depending on the local situation will be discussed briefly.

Very early, i.e. stage IA1, disease is relatively rare in developing countries and will usually be diagnosed within the frame of a screening programme. For stage IA1 disease, the risk of lymph node metastases is negligible. Standard treatment is simple hysterectomy. Conization is optional in case of further pregnancy wish. However, after

Conization, follow up with pap smear is warranted. If this is not realistic, hysterectomy is the treatment of choice.

For stage IA2 disease, the risk of lymph node metastasis is approximately 7%.\textsuperscript{22} Surgical treatment should consist of simple hysterectomy (or conization) and pelvic lymph node dissection.\textsuperscript{23}

For all other stages, the mainstay of treatment is radiotherapy, preferably in a combination of external beam radiotherapy and intracavitary brachytherapy, if available.

Recently, it has become evident that a combination with chemotherapy (cisplatin) is more effective than radiotherapy alone.\textsuperscript{24} However, maintaining the haemoglobin level at 11 g/dL or above is probably more important and also more realistic in low-resource settings than administering chemotherapy. The effectiveness of radiotherapy is not only enhanced by chemotherapy but also by an adequate haemoglobin level as radiotherapy is more effective in well-oxygenated tissues.\textsuperscript{25}

Early-stage disease (up to stage IB-IIA) can also be treated by radical hysterectomy and lymph node dissection if a surgeon with sufficient skills is available. The primary surgery approach has proven to be equally effective.\textsuperscript{26} However, in an estimated 25%, postoperative radiotherapy will be warranted, resulting in a more costly and prolonged treatment with a higher risk of side-effects.

Palliative care

For the majority of women in developing countries, curative treatment for cervical cancer is not realistic. This is due to late diagnosis as well as to lack of resources. However, health-care providers can still help these women by trying to control their symptoms.

Cancer pain is often grossly under-treated. This issue is of concern because more than 80% of patients with cancer pain find adequate relief through the use of simple drugs.\textsuperscript{27} It is advisable to start with paracetamol up to 3 g a day in three to six doses. If this is not sufficient, an NSAID (non-steroidal anti-inflammatory drug) should be added. The third step encompasses opioids. Opioids are inexpensive and effective. They should be administered every 4–6 h, but slow release morphine is administered 2–3 times daily. If the dose is too low, it should be increased by 50%. It is essential to add a laxative, as constipation is a side-effect of opioids in all cases.

Another common problem in advanced cervical cancer is vaginal discharge. This may be relieved by metronidazole tablets 2 × 500 mg daily or by vaginal irrigation. A relatively expensive but effective agent is topical metronidazole 0.8% gel. Alternatively, bismuth paracetamol gauzes or charcoal dressings may be applied.

Massive vaginal bleeding can be controlled by emergency radiotherapy, which is 100% effective in 12–48 h.\textsuperscript{28} However, the long-term prognosis of these patients is poor.

Ureteric obstruction occurs frequently in advanced cervical cancer patients. It will result in hydrenephrosis, and eventually ureaemia, resulting in ureaemic death. It may be an option to insert a nephrostomy. However, this will prevent the patient from dying the relative mild death by ureaemia. A few weeks to months later, she may die in uncontrollable pain. This dilemma should be discussed with all involved whenever the insertion of a nephrostomy is considered.

References

The use of ultrasonography in obstetrics in developing countries

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TROPICAL DOCTOR 2007; 37: 70–72

SUMMARY Ultrasonography in pregnancy is one of the most important advances in antenatal and obstetric emergency care. The benefits of diagnostic ultrasound in a resource-poor setting are well known and undisputed. Routine ultrasound can provide real benefit to patients when it is included in antenatal care programmes designed to improve maternal and neonatal health, and it should become a standard procedure in developing countries. Proper training of the antenatal ultrasound imager is very important. This should include training in ethics, use and misuse of ultrasonography as well as good technique and understanding of implications for clinical care to improve sensitivity. Training should be aimed not only at doctors but also at midwives who conduct most of the antenatal care and skilled deliveries in developing countries. Communication with patients and information about the limitations and benefits of ultrasound are essential to alleviate fear and to discourage irrational expectation and demand. Finally, routine antenatal ultrasound should be monitored closely for possible misuse, such as sex screening and selective abortion of normal female fetuses, and non-indicated overuse by health-care professionals for their own financial benefits.

References

5 Lowndes CM, Gill ON. Cervical cancer, human papillomavirus, and vaccination. BMJ 2005;331:915-16