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Review

Advances in colposcopy: new technologies to challenge current practice

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ABSTRACT

Colposcopy has a poor sensitivity to detect precancerous abnormalities of the cervix. These abnormalities will become less common after HPV vaccinated girls enter the screened population. However HPV-based screening is likely to result in more colposcopic referrals. Both these changes to cervical screening programs will reduce the incidence of high grade CIN and cervical cancer as well as the prevalence of high grade CIN presenting to the colposcopist. As a consequence the diagnostic performance of conventional colposcopy will be further challenged. This review aims to discuss leading technologies which are currently available as an alternative or in addition to colposcopy and may serve to improve the current colposcopic assessment of precancerous cervical abnormalities.

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Introduction

The pioneering work of Hans Hinselmann and Georgios Papanicolaou paved the way for a cervical cancer screening program. Initially Hinselmann's colposcope and Papanicolaou's vaginal exfoliative cytology were favored in isolation by differing regional or national screening services. Cervical cancer death rates did not improve until Scandinavia, Western Europe and North America introduced organized screening services capable of effectively detecting and treating cervical pre-cancer before progression to invasive disease. The success of the National Health Service cervical screening program over the last 25 years has meant that cervical cancer is now a relatively uncommon cancer in the UK. In 2010 there were 2851 new cases diagnosed, accounting for around 2% of all cancers among women, making it the 12th most common cancer overall in women in the UK [1] where it remains the most common cancer among women younger than 35, with about 700 cases diagnosed annually [2].

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The performance of a test depends upon the prevalence of the parameter being tested. The rarity of cervical cancer in modern cervical cancer screening programs may make the diagnosis of cervical cancer and pre-cancer more difficult by the diagnostic limitations of current colposcopic assessment. Perhaps Hinselmann's original design from almost 100 years ago requires reappraisal.

The future environment for colposcopy

The incidence of cervical cancer is expected to decline further in the developed world following implementation of human papillomavirus (HPV) vaccination and HPV-based screening. There is evidence that HPV vaccination is already reducing the incidence of high grade CIN within three years of establishing a population-based HPV vaccination program in Australia [3] and of high grade cytology within four years from the Costa Rica Vaccine Trial [4]. The three dose vaccination rate for 12 to 13 year old girls varies between 86 and 73% in England and Wales [5,6] dropping to less than 50% uptake for those 14 to 18 years of age [7,8]. Participation rates within the European Union for a full three dose schedule appears to be particularly high for vaccination where organized or highly compliant opportunistic cervical screening programs exist. The highest uptake rates were seen in Denmark, Portugal and the UK according to a recent European Centre for Disease Prevention and Control report and higher vaccination rates were noted in the youngest cohorts [9]. However it is worthy to note that only 10 of the 20 countries offering vaccination provided uptake data for this report. In Scotland and Wales the older vaccinated women have been invited for screening since 2010. Over the next generation general practitioners, practice nurses and junior gynecologists will not see many cases of overt cervical cancer and colposcopists will have limited expertize in diagnosing microinvasive or early invasive clinical disease. The consequences of vaccination upon colposcopic practice are difficult to determine with any clarity. HPV types 16 and 18 appear to be responsible for the majority of CIN3 lesions [10]. The incidence of cancer and the need for treatment for CIN may be reduced by at least 50% if there is uptake of vaccination of at least 80% of the eligible population [11].

Several reports have shown that the sensitivity for cervical cytology to detect high grade CIN appears to be consistently poorer than HPV testing in a screening setting. In a meta-analysis of 25 studies Koliopoulos et al. (2007) reported a combined sensitivity of hybrid capture II HPV testing to detect CIN2+ of 90% compared to cytology (threshold of atypical squamous cells of undetermined significance: ASC-US) of 73% [12]. More colposcopies would be anticipated with an HPV-based screening test positive rate of up to 16% [13–16] with an approximate doubling of the referral rate to colposcopy compared to that for current cytology-based screening [17]. A post implementation report of HPV-based screening in Italy revealed 11% (31/272) of colposcopy referrals yielded a diagnosis of CIN2+ following triage with ASC-US or worse cytology [18]. This is approximately one third of that seen for cytology based screening in Wales where no HPV testing is currently performed [19]. Such a low prevalence of CIN2+ in the population of colposcopy referrals may compromise colposcopic diagnosis of high grade CIN. Algorithms including HPV typing and other biomarkers may yet refine referral practice but the impact of such modifications upon colposcopic performance is currently unclear.

As a consequence of program developments, more colposcopies and less CIN2+ will mean that the positive predictive value (PPV) and sensitivity for colposcopy to predict high grade disease is likely to drop over the next 20 years.

The current environment for colposcopy

Although the diagnostic accuracy of colposcopy may become worse in the future, it is challenged now. Recent studies report a sensitivity of 49 to 61% for colposcopy to detect high grade CIN [20–25]. Published classification systems such as the Reid index tend to have a low sensitivity even when performed by expert colposcopists [26,27]. Diagnostic accuracy may depend upon the number of punch biopsies taken rather than who takes them [20,28]. The current method of examining the cervix to determine the extent of abnormality and whether any treatment is required is prone to considerable inter- and intra-observer variation in interpretation of results, particularly for low grade lesions [29]. Gage et al. found that 30% of CIN3+ was missed at initial colposcopy in the ASC-US and Low Grade Triage study [28]. This is likely to be because the current method of colposcopic assessment relies on a visual examination of the cervix which is subjective in nature. A technology that can improve diagnostic accuracy for cervical cancer clearly has the potential to impact on subsequent treatment decisions and improve patient outcomes [2].

Future advances in colposcopic assessment

There is a prospect of improving upon the subjectivity of colposcopy using optical or electrical biosensors which measure the altered appearance or electrical signature of dysplastic tissue compared to normal cervical epithelium. Electrical devices need contact with the host epithelium and so simultaneous visual assessment is not possible. Non-contact devices provide concurrent imaging. Five candidate technologies are discussed.

DySIS

DySIS (DySIS Medical Ltd, Livingston) is a digital video colposcope that also uses proprietary dynamic spectral imaging technology to measure the rate, extent and duration of acetowhitening of cervical epithelium to guide the colposcopist to the site of a possible biopsy. DySIS therefore replaces the conventional colposcope and no further colposcopy is required. A colored grading of the acetowhite change (or DySISmap) is superimposed on a live color image of the cervix to help the colposcopist determine the presence and severity of an abnormality and assist in the selection of the site for biopsy.

The DySIS digital colposcope consists of a monocular optical head with a light source providing uniform illumination, and magnification optics linked to a digital camera. It also includes a computer and a touch-screen monitor for image and data display. It has an integrated database for recording of all patient information, images and colposcopic findings. A single use speculum is required for DySIS and differs from standard specula used in colposcopy in that it has an additional shaft that connects it to the optical head of the colposcope. As a consequence the patient has to be completely still during the course of her colposcopy. Furthermore, the duration of examination including a colposcopy is probably slightly longer than that of a standard colposcopy. This is because in order to calculate the DySISmap a full dataset of 23 images is collected over two to three minutes but during this time the colposcopist would be performing some of the standard visual assessment. Colposcopists have to become used to looking at the DySIS computer screen rather than a binocular eye-pieces and such re-orientation may add to training time. Even so, colposcopists become familiar with the use of DySIS and interpretation of its findings in up to 20 examinations.

Studies with DySIS assisted colposcopy have shown promising results [23,30]. DySIS colposcopy had a statistically significant higher sensitivity for identifying CIN 2+ than with conventional