Clinical Review

Clinical Review identifies issues in the medical literature of interest to clinicians in Africa. Essential references are given at the end of each section

STI Review

The World Health Organization: towards ending sexually transmitted infections 2016–2021

The World Health Organization (WHO) recently updated their global strategy on responding to sexually transmitted infections (STIs) for 2016–2021, with specific goals, targets, guiding principles and priority actions.[1] This strategy is aligned with the United Nations 2030 Agenda for Sustainable Development, most specifically Goal 3: Ensure healthy lives and promote well-being for all at all ages.[2] In addition to providing the current global status of STIs, the strategy presents three organising frameworks: Universal Health Coverage (UHC), a continuum of STI services, and the public health approach focusing on preventing disease, promoting health, and ensuring quality of life among the population as a whole. It sets out specific measurable goals for 2020 and 2030, with the ultimate goal of ending the STI epidemics as major public health concerns. This is defined in the strategy by the reduction in cases of *Neisseria gonorrhoeae* and *Treponema pallidum*, as well as by the elimination of congenital syphilis and of pre-cervical cancer lesions through the high coverage of human papillomavirus (HPV) vaccines.

Full achievement of the strategy by 2021 is estimated to cost US$18 200 million, almost all of which is for implementing priority interventions in 117 low- and middle-income countries, with $53million for global-level technical support, research and advocacy by WHO and partners. The greatest expenditures are for STI vaccination ($3260 million), STI screening ($3690 million), adolescent chlamydia screening ($2540 million), and antenatal syphilis screening ($1400 million). Clinical STI management is estimated at $3000 million, with $818 million for service delivery, and $1400 million for diagnostic testing for gonorrhoea and chlamydia. The $53 million for global-level activities funds the development of point-of-care tests to improve affordable STI screening, operational research, and guidance on STI surveillance. Sub-Saharan Africa, which bears 40% of the global burden of STIs, is estimated to require 44% of the estimated services and 30% of the global control costs. The strategy relies on countries' health systems to provide the funding for STI control programmes, with some support for HPV vaccination from national immunisation programmes. The strategy also recommends that STI programmes leverage funds from HIV prevention, maternal, child and adolescent health and immunisation budgets.

Updated STI treatment guidelines – gonorrhoea

The WHO has also updated its guidelines for the treatment of gonorrhoea, syphilis, chlamydia, and herpes simplex virus 2.[3–6] These updates, the first on STIs since 2003, provide treatment guidelines based on the latest data. New treatment protocols are needed in the face of increasing antimicrobial resistance to common STIs. Of all the new guidelines, perhaps the most urgent need is for updates in the treatment of gonorrhoea. While it is now widely known that the bacteria which causes the disease, rapidly develop resistance to the antibiotics commonly used for treatment (which have included sulphonamides, penicillins, cephalosporins, tetracyclines, macrolides and fluoroquinolones), there is great need for all countries to update national treatment protocols that reflect local antimicrobial resistance (AMR). The new WHO guidelines no longer recommend the use of quinolones to treat gonorrhoea in any scenario. The updated guidelines provide six specific treatment recommendations for conditions caused by *N. gonorrhoeae*, including genital, anorectal, and oropharyngeal infections in adults and adolescents, and ophthalmia neonatorum in newborns.[3] Where local resistance data is not available, WHO recommends dual therapy treatment for genital or anorectal gonorrhoea in adults and adolescents with ceftriaxone 250mg intramuscular (IM) as a single dose PLUS azithromycin 1g orally as a single dose, OR cefixime 400mg orally as a single dose PLUS azithromycin 1g orally as a single dose. If local data confirms susceptibility to the antimicrobial, single therapy can include ceftriaxone 250mg IM as a single dose, OR cefixime 400mg orally as a single dose, OR spectinomycin 2g IM as a single dose. There are further treatment guidelines for retreating after treatment failure, for oropharyngeal infections, and for prophylaxis and treatment of ophthalmia neonatorum.

As indicative of how rapidly *N. gonorrhoeae* evolves, the US Centres for Disease Control (CDC) reported late in 2016 that a cluster of gonorrhoea infections from Hawaii showed decreased susceptibility to ceftriaxone and very high-level resistance to azithromycin – the two-drug regimen currently advised for use by the CDC and WHO.[7] However, those two drugs continue to be the recommended treatment protocol for gonorrhoea in the United States. Moreover, the CDC emphasised that the system in place is working: providers diagnosed and treated infection, public health officials quickly detected resistance, and cutting edge lab technologies were used to track spread of the disease and treat people linked to the cluster.

WHO has been supporting surveillance of gonococcal antimicrobial resistance since the 1990s, yet surveillance in sub-Saharan Africa is very limited.[8,9] As syndromic management of STIs increased, the collection of genital specimens for testing declined, as did the skills needed by medical and laboratory staff to collect and process samples.[8] WHO has invested in the Gonococcal Antimicrobial Surveillance Programme (GASP),

which supports a network of laboratories worldwide to coordinate gonococcal antimicrobial resistance monitoring and provide data to inform treatment guidelines.[10,11] However, there has been no GASP laboratory in Africa since February 2012, and prior to that the only participating laboratory was the Sexually Transmitted Infections Reference Centre, National Health Laboratory Service, in Johannesburg, South Africa.

While widespread surveillance in Africa is absent, there have been small studies that show the local status of gonococcal AMR. A cross-sectional study of 186 STI-suspected patients at a hospital in Ethiopia found that 11.3% tested positive by culture for gonorrhoea.[12] Men were four times as likely as women to be infected. All *N. gonorrhoeae* isolates proved susceptible to ceftriaxone and cefoxitin, but all were resistant to penicillin and tetracycline. A surprising 28.6% of isolates were resistant to ciprofloxacin. Such studies show the risks of prescribing antibiotics according to syndromic management protocols without antimicrobial testing.

Surveillance of gonococcal antimicrobial resistance is costly and dependent on laboratory testing. Treatment failures and untreated partners contribute to increasing antimicrobial resistance. Pharyngeal gonorrhoea, which is often asymptomatic, has been seen as the site of emerging antimicrobial resistance.[13] Diagnosis of gonorrhoea infection is increasingly carried out using nucleic acid amplification (NAAT) testing of urine instead of culture of urethral or cervical/vaginal specimens, which severely limits the samples available for antimicrobial testing.[14] Even where culture testing is available, it can take 48 hours to obtain results with antimicrobial susceptibility. There is need for rapid molecular tests that can detect antimicrobial resistance. There has been some progress in developing novel ways of detecting antimicrobial resistance from urine samples. One study extracted DNA from 13 *N. gonorrhoeae* NAAT-positive urine specimens and successfully sequenced the entire genome of the bacteria.[15] Comparing the DNA found in the samples with a reference genome revealed mutations known to be associated with antimicrobial resistance. By sequencing the entire genome, novel mutations can also be identified. While this testing is far too expensive for routine public health surveillance, it demonstrates the potential for antimicrobial testing when culture is not available.

Another study used molecular testing on DNA isolates to predict susceptibility to ciprofloxacin.[16] Of 76 six urine and swab specimens positive for *N. gonorrhoeae*, 71% were genotyped. Mutations in the gene known to confer ciprofloxacin resistance were identified in specimens and resistance was confirmed through culture. The molecular test took 1.5 hours to perform, which could enable healthcare providers to test and treat the same day. In the US, an estimated 19.2% of *N. gonorrhoeae* isolates are resistant to ciprofloxacin. Having rapid results of antibiotic-specific resistance or susceptibility would allow healthcare providers to prescribe alternative treatments, and potentially delay emergence of ceftriaxone resistant *N. gonorrhoeae*.

There is some good news on potential treatments for gonorrhoea. In Uganda, a study of leaf and root extracts of Cassia alata (Caesalpiniaceae) found both inhibited growth of *N. gonorrhoeae* isolated from a treatment resistant case.[17] While this plant has been widely used in home remedies, and is known to have antimicrobial effects on bacteria, fungi and amoeba, this was the first test of the plant leaf and root activity on the bacteria in vitro. Further testing is needed to determine the active components of the extracts and how best to isolate them from the plant material. In another study, a novel oral antibiotic was tested on 179 participants with confirmed urogenital gonorrhoea.[18] This phase II trial of ETX0914, the first of its class of antibacterial agents, inhibits DNA synthesis. The study found that all patients in the 3g ETX0914 arm (47/47) and 98% of patients in the 2g arm (48/49) were cured of the infection. Few patients (21/179) reported side effects, which were mostly mild and primarily gastrointestinal. ETX0914 is continuing through clinical trials.

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Family Medicine Review

For one reason or another, a succession of articles that address a range of mental health issues caught my eye over recent months. This will thus be the major, but not exclusive focus of this review.

Intimate partner violence

Domestic violence, now more correctly called Intimate Partner Violence (IPV), which is part of a broader category of Gender-based Violence (GBV), is a major global scourge, and particularly problematic in Africa, with an estimated one in three women globally experiencing physical or sexual violence.[1] A recent US report of a 20-year cohort follow-up study of women living with HIV found that 47% of women experienced IPV;[2] the study highlighted the importance of screening for the problem. Also in 2016, a study from Kano in Nigeria found that 42.2% of women attending a general outpatient clinic reported that they experienced IPV in the preceding year; this study also emphasised the importance of screening.[3] A study published earlier this year amongst both men and women in an outpatient setting in rural Uganda demonstrated the co-occurrence of depression, IPV, and alcohol use, which in turn was associated with greater HIV risk,[4] with a Tanzanian study showing that women living with HIV/AIDS who experience IPV show poor adherence to antiretroviral medication and attend the care and treatment clinics less frequently.[5] The association of IPV, HIV and mental health are well described.[6] A wide range of broad-based interventions to address IPV in the context of HIV in Africa have been summarised in a recent review of the literature.[7]

Many women with IPV are missed in primary care clinics. As noted above, screening is essential. The challenge is to identify an appropriate screening tool that busy clinicians, especially in primary care, can incorporate into their daily practice. A commonly used validated screening tool in family practice is the Woman Abuse Screening Tool (WAST), which consists of eight questions.[8] A recent study from South Africa evaluated a two-question version in the detection of IPV in a primary healthcare setting, known as the WAST-short.[9] The authors assessed whether the first two questions of the longer tool, which have been successfully used in other contexts, could be used in their context. The questions used in the WAST-short are:

1. In general, how would you describe your relationship with your partner?
   a) A lot of tension
   b) Some tension
   c) No tension
2. Do you and your partner work out arguments with...
   a) Great difficulty
   b) Some difficulty
   c) No difficulty

They found that, while the specificity of the test was high (98%) its sensitivity was insufficient to be an ideal screening tool (45,2%), possibly because of how the Eurocentric questions were interpreted in the outpatient context in South African primary care. There is a need for further validation in the African context, or the identification of an alternative short tool that clinicians can use; in the meantime, use of these questions, with appropriate local adaptation, would certainly be better than nothing.

Challenge of providing care to patients with mental health problems

Globally, mental, neurological, and substance use disorders represent a significantly high component of ill-health internationally, increasing between 1990 and 2010 from 7.3% to 10.4% as a proportion of the global disease burden. Despite this, most African countries are taking relatively little action to address the healthcare needs of people with such disorders, given that 0.5% and 1.9% of the health budget goes to mental health in low-income and lower-middle-income countries respectively, and less than 1% of the developmental assistance for health in such is allocated to mental health.[11] In this context it is interesting to read a report just published on six low- and middle-income countries (LMICs) participating in the emerging mental health systems in LMICs (Emerald) project, four of which are in Africa, *viz*. Ethiopia, Nigeria, South Africa and Uganda (with the remaining two being India and Nepal). The authors looked at existing system level resources for integrating mental health into primary healthcare (PHC). Most of the countries were found to be allocating inadequate budgets for mental health, with South Africa (5%) and Nepal (0.17%), to be lacking robust policies to support mental health care, and to have inadequate resources to support integration such as human resources and health facilities for mental health services.[12]

Confirming the above, a study on mental health nurses (MHNs) in rural South Africa found that in rural primary care facilities MHNs are employed at a rate of 0.68 per 100 000 population compared to a national rate of 9.7 per 100 000 population, in a context of severe shortages of medical practitioners who focus on mental health and a near absence of specialist psychiatrists in rural areas.[13] This accords with a 2016 report from Nebraska in the USA where rural areas face significant challenges in recruiting and retaining behavioural healthcare professionals, defined as psychiatric prescribers, independent behavioural professionals, mental health practitioners, and addiction counsellors.[14] It is vital that as clinicians we pay greater attention to mental health problems and develop the necessary skills to care for our patients more effectively.

In Australia, one approach to addressing mental ill health in rural and remote areas, recently described in the literature, was the Mental Health Academic (MHA) project, established in 2007 to 'increase access to mental health services, promote awareness of mental health issues, support students undertaking mental health training and improve health professionals' capacity to recognise and address mental health issues'.[15] There is certainly a need for such initiatives across countries in Africa, where limited services are highly concentrated in large cities.

Two papers published over the last six months high-

lighted a key area of mental health in rural communities, *viz*. dementia in older people. One from Canada looking at healthcare provider perspectives notes the challenges of dealing with patients suffering from dementia and delirium in the emergency department. This paper, which is worth a read, concludes with the injunction to healthcare professionals to seek input from caregivers of elderly patients regarding any altered functional status, to change triage training to include knowledge of geriatric care and to develop policies that create elder-friendly emergency department environments.[16] The other, from Australia, describes a programme to train volunteers to provide personal support to these patients with dementia and/or delirium. The authors conclude it is feasible to develop and sustain such a relatively inexpensive programme to improve quality of person-centred care for such people in a rural hospital.[17]

Two related snippets

Postnatal depression affects about 10–15% of mothers in the first year after giving birth. *The Annals of Family Medicine* late last year published a meta-analysis on the effectiveness of psychological interventions for postnatal depression. The authors screened 5919 articles to identify 10 studies that met their inclusion criteria, which studies used a range of intervention, including cognitive behavioural therapy, interpersonal therapy and counselling. The meta-analysis showed that such interventions resulted in lower depressive symptomatology than control both immediately after treatment and at six months of follow-up, without significant differences between the various types of therapy, AND led to improvements in adjustment to parenthood, marital relationship, social support, stress and anxiety.[18] It is thus essential that patients with postnatal depression are not simply medicated, but are referred to whatever psychological support services may be available.

A study from Botswana on depression in caregivers of malnourished children piqued my interest because I remember as a medical student in the 1980's being fascinated by a movie where researchers had used highly innovative technology to splice 16mm film longitudinally and join it together so that one could see two mother-child dyads at the same time, one with a malnourished child and one with a well-nourished child, in order to observe the interaction between mother and child, which was startlingly different. The recent Botswana study found that malnourished children in the six-month to five-year age group were significantly more likely to have depressed primary caregivers than non-malnourished children (odds ratio = 4.33; 95% CI: 1.89, 9.89).[19] It is thus important to address the mental wellbeing of caregivers when dealing with malnutrition in their children. Clinically, how much is cause and how much effect is not important—it needs to be managed.

Chronic care and the diabetic foot

Chronic disease is a theme I return to repeatedly. Before addressing the topic of the heading, I wanted to mention an interesting paper on an issue that is close to me, which is that of integrated chronic disease management (ICDM). While this does not necessarily represent implementation of all the principles of chronic illness care that I have called for,[20] it is an important attempt to address such issues at a systemic level. Mahomed et al describe the South African ICDM model, which consisted of four components (facility reorganisation, clinical supportive management, assisted self-supportive management, and strengthening of support systems and structures outside the facility) that were implemented in 42 primary healthcare clinics, and which they evaluated in terms of sustainability, with a view to improve the operational efficiency and patient clinical outcomes. They report significant challenges with implementation that threaten its sustainability, despite many perceived benefits, which included less than optimal involvement of clinical leadership (doctors and senior professional nurses), negative behaviour of staff, limited flexibility of the model, and infrastructural limitations.[21] It is hoped that many such models could be developed and tested in Africa.

So I turn to one specific area of chronic illness care. Clinicians know that foot screening is an important part of the care of patient with diabetes mellitus, as it prevents significant morbidity, loss of function and mortality from complications. However, screening for foot problems in such patients is frequently neglected. Allen et al reported on a quality improvement project aimed at educating healthcare workers in a PHC to increase such screening practices. Confidence in conducting foot screening improved markedly after training, and diabetic foot screening practices increased from 9% in 2013 to 69% in 2014 with a significant improvement in the number of diabetic patients screened.[22] This demonstrates that focused attention by clinicians can make a difference. The paper also describes an approach to quality improvement, using strategic planning with appreciative intent based on a strengths, opportunities, aspirations and results (SOAR) analysis, that showed promise.

This study is particularly important, given the poor knowledge that most patients have of significant factors for all types of diabetic foot disease, according to a local survey in Durban, South Africa, which also found, incidentally, the clinical management of the disease to be poor.[23]

Two final snippets

Very little is known about developmental screening amongst children in most of Africa, despite milestones being included on most road to health charts. It is thus interesting to read an audit of practices aimed at monitoring the development of young children in remote Aboriginal health services.[24] Reviewing practices in two communities, the authors found that developmental checks were more likely among children who attended services regularly, thus suggesting that the overall recorded prevalence of developmental difficulties (21% and 6%) is likely to be low, and that a suboptimal number of medical records had any evidence of a developmental check (79% and 59%), with little indication of how assessments were undertaken, and only one record noting the use of a formal developmental screening measure across both communities, despite this being recommended. One can only guess what the situation is across communities in Africa. Given the

major difference that early intervention can have on the future health, education and economic status of children, it is time that serious attention was given to this. In order for that to happen, clinicians must take the lead and become agents of change.

A just published article by Mji et al describes four case studies of people with disabilities from four diverse low-resource contexts in South Africa (rural, semi-rural, farming community and peri-urban) looking at the challenges of access to health services experienced by people with activity limitations.[25] The case studies demonstrate that, despite primary care services being free in public health facilities, access to public health services can be difficult, with transport being a major challenge and costs such as transport, personal assistance and food (given that a visit to a health centre may take the whole day) also being a significant obstacle. This vulnerability of people with disabilities must be taken into consideration by healthcare professionals in planning ongoing care.

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Ophthalmology Review

Managing ocular surface squamous neoplasia

The most common ophthalmic cancer in Africa is ocular surface squamous neoplasia (OSSN). This usually presents as a white or pink fleshy lesion at the limbus, and may well be encountered by PHC workers, as well as ophthalmologists and specialist eye health personnel. Researchers from Nairobi and the London School of Hygiene and Tropical Medicine have been conducting a clinical trial of the management of OSSN in Africa, which was published in 2016. I want to look at some of the research they have presented over the last few years.

OSSN is more common in Africa than in any other region.[1] The research team conducted a systematic review to examine the reported incidence of the condition around the world. They caution that the results should be treated with a degree of scepticism, as the data comes mostly from cancer registries, which may not be completely reliable. The countries with the highest incidence are also the countries with the least access to histopathology facilities, which means that the tumours are not always diagnosed, or placed on the registry. However, despite these limitations, the conclusion of the review is very clear—the incidence of OSSN in Africa is about 1.3/100 000 per year, compared to around 0.05 in Europe and North America.

In Africa, OSSN appears to occur at a much earlier age, and occurs at a fairly similar rate in men and women. The disease most frequently occurs in people in their 30's. In temperate and sub-tropical countries

(e.g. Australia) incidence is highest in men in their 60's. Looking at historical data, this used to be the case in Africa as well. In the 1960's, the mean age of patients with OSSN was 48, and the majority were men. Today, the mean age at presentation is 38 in Kenya, 37 in South Africa and 39 in Tanzania, compared to 64 in the US. The male:female ratio is at least 2:1 in the US and Australia, compared to about 1:1.2 in African countries.

Not only does OSSN occur more frequently, and at a younger age in Africa, it is also becoming more common. One study from Kampala showed that the incidence in Uganda was ten times higher in the 1990's than the 1980's.

What is the explanation for the very different pattern of disease in Africa? One obvious risk factor is exposure to sunlight. People who are working outdoors, in strong sunlight are more likely to develop OSSN. There does appear to be a weak link between the time spent in strong sunlight and the risk of OSSN. In Europe and North America, fewer people work outside, and there are fewer sunny days.

However, the major reason for the difference in Africa is HIV. A meta-analysis of six case control studies showed that people infected with HIV were six times more likely to develop OSSN than non-infected individuals. About 60–70% of people with OSSN in Africa have HIV. HIV-related OSSN tends to be larger, and may be more likely to recur after excision. Although the evidence for a link with HIV is strong, there is no direct evidence linking OSSN and immunosuppression, as there does not seem to be a correlation between CD4 counts and the risk of OSSN. Data from the US suggests that highly active antiretroviral therapy (HAART) does not affect the risk of developing OSSN.

The first learning point of this article is that any patient presenting with OSSN should be encouraged to have HIV testing, as this may be the first manifestation of HIV/AIDS.

OSSN is usually unilateral. Patients may complain of irritation or foreign body sensation, caused by the irregular ocular surface. On examination there may be a raised pink fleshy growth at the limbus (the junction of the conjunctiva and cornea), or a white plaque of keratinised squamous epithelium. There may be a prominent blood vessel (feeder vessel) leading to the lesion. In advanced cases, the entire globe may be replaced by a fungating orbital mass. It is most commonly found in the exposed conjunctiva between the upper and lower eye lids. It can look very similar to benign lesions such as pingueculum and pterygium. These benign lesions affect the nasal limbus, but OSSN can be found at any site.

As part of the clinical trial, the authors recruited 496 patients with ocular surface lesions from four eye clinics in Kenya.[2] All lesions were photographed, and then excised and sent for histopathology. Thirty-eight per cent (38%) were OSSN, 36% pterygium, and 19% actinic keratosis. Among patients with OSSN, over 70% had HIV. The authors identified a number of clinical features, such as lesion location, size, leukoplakia, feeder vessel, inflammation, pigmentation, gelatinous appearance, and corneal involvement. Six final year ophthalmology residents at Kenyatta National Hospital were asked to decide if these clinical features were present, absent, or difficult to determine. There was fair inter-observer agreement between the ophthalmology residents for the presence or absence of the clinical features.

Some of these features were strongly linked to malignancy. For example, lesions with feeder vessels (O.R. 5.8), severe inflammation (O.R. 42.3), leukoplakia (O.R. 2.6), or involving the cornea (O.R. 2.7) were significantly more likely to be malignant than benign. However, there was considerable overlap, and all of these 'high risk' features were found in both benign and malignant lesions. Unsurprisingly, the ophthalmologists were not very good at distinguishing benign from malignant lesions on the basis of the clinical appearance. A clinical diagnosis of OSSN had a sensitivity of 86%, specificity of 60%, and a positive predictive value of 54%.

The second important learning point is that it is very difficult to distinguish benign and malignant lesions purely on their clinical appearance. This means that all suspicious ocular surface lesions should be excised and sent for histopathology.

The final paper in this series is the clinical trial of treatment for OSSN.[3] The mainstay of treatment remains excision, with a 3mm margin and direct closure of the conjunctiva. This is usually done under an operating microscope. However, its effectiveness is limited by tumour recurrence, which has been reported to be as high as 67%. In order to reduce the risk of recurrence, a number of adjuvant treatments have been tried. These include cryotherapy, radiotherapy, mitomycin C and 5-fluorouracil (5-FU). However, there is little evidence to support any of these adjuvant therapies. Furthermore, cryotherapy and radiotherapy are unlikely to be widely available in Africa. There is one randomised trial of mitomycin-C (MMC) in OSSN. This comes from Australia, and showed that MMC is effective as a treatment for OSSN. However, MMC is costly, and has to be kept at a low temperature. It is also toxic, and has been associated with scleral necrosis when used for pterygium. There are no trials of adjuvant treatment in patients who also have HIV.

Patients with suspicious ocular surface lesions were enrolled from four clinics in Kenya. Only those with histologically proven OSSN were included in the trial. Other inclusion criteria were attendance for follow-up at two months, and complete healing of the site of excision. Patients were excluded if they required more extensive surgery, if they had previously been treated with anti-metabolites, or if they were unable to return for follow-up.

Four weeks after surgery, patients returned to the clinic, and were given the results of the histology. Those with OSSN were randomised to either 1% 5-FU drops or methylcellulose drops. Patients, clinicians and study personnel were masked to the treatment allocation. The drops were given four times per day for four weeks from the date of randomisation, and this was monitored with a treatment diary recorded by the participants. Follow-up visits were scheduled for one, three, six, and 12 months after randomisation, and every effort was made to ensure complete follow-up.

The primary outcome was lesion recurrence, which was confirmed by excision of the recurrent lesion. Secondary outcomes included adverse effects of the 5-FU.

One hundred and eighty-seven (187) patients had OSSN. Eighty-nine (89) were excluded. Forty-one (41) were unable to return for follow-up. Twenty-four (24) had extensive disease involving more than two quadrants, 16 did not return for surgery, and another eight patients were excluded for other reasons. Ninety-eight (98) patients were included in the trial. Forty-nine (49) were randomised to 5-FU or methylcellulose drops. Two patients were lost to follow-up in each group. The two groups were well-matched. The only significant difference in the baseline characteristics was that 42% of the placebo group were on HAART compared to 22% of the 5-FU group.

Recurrence occurred in five (11%) of the 5-FU group and 17 (36%) of the placebo group (O.R. 0.21, 95% c.i. 0.07 – 0.63, p=0.01). The relative risk reduction was 71% and the absolute risk reduction was 25%, which means that one recurrence would be prevented for every four patients treated with 5-FU. Tumour size also influenced the recurrence rate, with larger lesions more likely to recur. However, tumour grade and completeness of excision (confirmed by absence of tumour at the margins) did not affect the risk of recurrence. Adverse effected were more common in the 5-FU group than in patients treated with methylcellulose alone. Epiphora and irritation were common during 5-FU treatment, and a few patients developed irritation of the skin and eyelids. However, no adverse effects persisted after treatment was completed.

The treatment 5-FU is on the World Health Organization essential drugs list. It is already widely used in ophthalmology to improve outcomes of glaucoma surgery. It is inexpensive and can be stored at room temperature. Topical 5-FU treatment should be deliverable even in a healthcare system with limited resources.

The final learning point is that all patients having OSSN lesions excised, should be given four weeks of 1% 5-FU four times per day when the site of the lesion has healed.

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