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

Medicine Review

Aspirin – risks and benefits

Traditionally used only as an analgesic, the humble and inexpensive drug aspirin (acetyl salicylic acid) has had a great resurgence in use over the last 20 years or so as a preventer of vascular disease. Its use is now well established and firmly evidence based in the context of 'secondary prevention', i.e. in definite atherosclerotic arterial diseases – coronary artery disease (CAD), peripheral vascular disease (PVD) and cerebrovascular disease (CVD). A dose of only 75 mg per day is effective at significantly reducing the risks of future vascular events, and treatment should be life long. Interestingly, there is also a suggestion of a reduction in overall cancer mortality in patients treated with long-term aspirin.

Arterial atherosclerotic disease is less commonly seen in many parts of Africa than in Western countries, However, with increasing urbanisation and westernisation, rates are increasing and the indications for aspirin treatment are also rising.

A major ongoing controversy, however, concerns the value of aspirin in primary prevention, i.e. preventing vascular disease before it has happened. There is some evidence that aspirin in this situation can reduce the risk of non-fatal myocardial infarction (MI), but not overall cardiovascular mortality. A recent meta-analysis, however, suggests that any benefits are offset by the raised risk of bleeding events. The analysis was recently reviewed in a *British Medical Journal* editorial,[1] and included nine randomised placebo-controlled trials involving nearly 103 000 patients. All studies involved the use of aspirin in persons without known cardiovascular disease. Over a mean follow-up period of 6 years there was a 10% reduction in cardiovascular events in those taking aspirin, mostly due to fewer non-fatal MIs. However, there was no significant reduction in cardiovascular deaths, or malignancy-related deaths. Importantly, however, those on aspirin had a 31% higher rate of 'non-trivial' (i.e. potentially serious) bleeding events.

The authors emphasised that aspirin for secondary cardiovascular prevention remained justified, but that their evidence argued against routine use for primary prevention. Giving aspirin to those without cardiovascular disease should, therefore, be decided on an individual basis, and should be reserved for those at particularly high cardiovascular risk. For example, in Caucasian groups, diabetes with hypertension is often considered such an indication.

No similar trials have taken place in Africa, however, and it is far from certain that the results of this new meta-analysis can be transposed to black African populations, who mostly have a significantly lower cardiovascular risk than white and Asian races.

Tuberculosis – continuing problems

Tuberculosis (TB) continues to be a major health problem globally, as it has been for centuries. Many years ago, a very experienced and accomplished physician colleague of mine in Africa used to remark to medical students that 'tuberculosis is a disease of antiquity, but not of the past.'

There are mixed messages at present coming from TB epidemiological and outcome figures. There is evidence of positive improvements, with a 40% reduction in mortality over the past 20 years, and a total of 46 million patients with TB cured in the last 15 years.[2] However, TB has still killed 1.45 million people since 2012, and about half a million people have drug-resistant disease.[3]

A major problem reflected by these figures is that positive progress varies greatly geographically. For example, incidence and outcome has improved greatly in China, but in most African countries TB remains a major health problem and killer. Control programmes are also mainly dependent on external aid programmes, which in the long-term is not sustainable. A recent hope has been that community-based isoniazid (INH) treatment in high-risk populations may reduce TB occurrence, but studies from South Africa are suggesting that this strategy is no better than routine case finding and targeted therapy.[3]

Future progress depends on political will, external aid, and new drug development. Also, as has always been the case, background strategies must include socio-economic development, improved housing, less overcrowding, better nutrition, and vigorous HIV control programmes.

Bad news on malaria?

Over the last few years there has been a significant reduction in malaria mortality – about a 30% reduction over the last 8 years.[4] Though this improvement is not doubted, new figures suggest that the overall mortality burden is much higher than previously thought. The work is by a respected group of epidemiologists from Seattle, USA, and was published recently in the *Lancet*.[2] Spanning a 30-year period from 1980 to 2010, the workers used multiple data collection techniques for collecting mortality data in malaria-endemic countries. As well as standard death registration records, verbal autopsy data were also collected.

The major finding was that global malaria deaths rose from 0.99 million in 1980 to a peak of 1.82 million in 2004, decreasing to 1.24 million in 2010. The pattern in Africa was similar (0.49 to 1.61 to 1.13 million over the same time frames). These figures are considerably in excess of current World Health Organization (WHO) estimates, and the underestimate was especially marked in adults.

An accompanying editorial points out that the global

mortality for 2010 of 1.24 million is about twice the WHO estimate for the same year of 0.65 million.[5] One area of agreement is the 30% reduction in mortality since the peak in 2004, but the actual number is widely discrepant. Who is right? Murray and colleagues are an experienced group using robust methodology, and whatever is the truth, WHO need to examine this report carefully and consider its implications for future malaria control programmes.

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Paediatrics Review

Hygienic umbilical cord care – antiseptics

In low-income countries, especially where home deliveries are in unhygienic conditions, infections account for about half of the neonatal deaths.[1] In a case-control study of 23 246 infants in Nepal, there were 392 deaths and odds of all-cause mortality were 46% higher among infants with umbilical sepsis extending on to the abdominal skin.[2] At delivery, after the umbilicus is cut necrotic Wharton's jelly is the most vulnerable site for colonisation by bacteria. These include staphylococci, streptococci and Gram-negative organisms, e.g. *Escherichia coli* and *Klebsiella* spp. If substances such as cow dung are applied to the cord, an even wider spectrum of pathogens are expected including tetanus spores. Rarely, maggots may cause umbilical sepsis.[3]

A study was undertaken in Sylhet, Bangladesh involving all married women of reproductive age (15–49 years).[4] In one arm, the home-care group, community health workers (CHWs) identified pregnant women, made two antenatal home visits to promote birth and newborn care preparedness, and then made postnatal home visits to assess newborns on the 1st, 3rd, and 7th days of life. Sick neonates were treated or referred. In the community-care arm, birth and newborn preparedness and care seeking was promoted through group sessions only. A comparison arm had no intervention. There were 14–16 000 live births in each of the three groups. In the last 6 months of the 30-month intervention neonatal mortality (NNM) rates (per 1000 live births) were 29.2, 45.2, and 43.5, respectively, in the three arms. Neonatal mortality was reduced by 34% (Confidence interval (CI) 0.47–0.93) in the home care arm compared with the comparison arm. There was no reduction in mortality in the community arm.

One of the main approaches to reduction in neonatal infection in home deliveries is the promotion of clean delivery kits. Data from the control arms of three previously conducted cluster randomised controlled trials (RCTs) undertaken in rural Bangladesh, India, and Nepal were analysed to examine the association between clean delivery kit use or clean delivery practices and NNM in home births.[5] The kits contained soap, razor, plastic sheet (to put under the mother), string, gauze, and instructions (in Government kits only). In addition, in Nepal a plastic rupee coin was included as a surface on which to cut the cord (a sign of good luck!). Using pooled data, kit use was associated with a relative reduction in NNM (adjusted odds ratio (OR) 0.52, 95% CI 0.39–0.68). Although use of a clean delivery kit was not necessarily accompanied by clean delivery practices, using a plastic sheet during delivery, a boiled blade to cut the cord, a boiled thread to tie the cord and antiseptic to clean the umbilicus were each significantly associated with reduction in mortality independent of kit use. Each individual clean delivery practice was associated with a 16% relative reduction in NNM (OR 0.84, CI 0.77–0.92). Using a clean delivery kit was associated with neonatal survival in India and Bangladesh but not in Nepal. However, only a small number of participants used a kit in Nepal (335). Using kits did not guarantee clean delivery practice as, for example, in India hand washing with soap prior to delivery occurred in only 40% of births where the kit was used. Few users took out the instructions for the kit and when they did they had difficulty understanding them. Kits were not necessarily free (some women or women's groups made up their own). Costs (in US$) were as follows: India (0.44), Bangladesh (0.27), and Nepal (0.40) which may be prohibitive for the poorest families. One limitation of this study was recall bias as women were not interviewed until about 6 weeks after delivery.

WHO advises 'dry cord care' as follows: wash hands before and after cord care, put nothing on the stump, fold nappy below stump, keep stump loosely covered with clean clothes, if stump is soiled wash with water and soap and dry with a clean cloth.[6]

Value of chlorhexidine

A Cochrane Systematic Review analysed RCTs of topical cord care compared with no topical care.[7] Twenty-one studies (8959 participants) were included. All were undertaken in hospital and all but one (Thailand) were from high-income countries which is reflected in the fact that no systemic infections or deaths were observed in any of the studies. No difference was demonstrated between cords treated with antiseptics compared with dry cord care or placebo. Antiseptics prolonged the time to cord separation.

Three recent RCTs examine the benefit of application of chlorhexidine (CHX) to the cord in prevention of omphalitis and reduction of mortality in low-income countries.[8–10] A trial in Sarlahi, Nepal randomised three groups of newborn infants (approximately 5000 infants in each group) to: (a) application of 4% CHX; (b) cleaning with soap and water; and (c) dry cord care.[8] In (a) the cord was cleansed by health workers in the home on days 1–4, 6, 8, and 10. In all the study groups the cord was examined for signs of infection (pus, redness or swelling) on these visits and on follow-up visits

on days 12,14, 21, and 28. Frequency of omphalitis by all above criteria was reduced significantly in the CHX group. Severe omphalitis was reduced by 75% in the CHX group (13/4839 neonatal periods) compared with dry cord care (52/4930). Neonatal mortality was reduced by 24% in the CHX group overall (not statistically significant) and by 34% for infants enrolled within the first 24 hours, which was statistically significant (incidence ratio 0.66, CI 0.46–0.95).

A RCT in Sylhet, Bangladesh, compared three groups: (a) single cleaning with 4% CHX as soon after birth as possible; (b) daily cleaning for 7 days after birth; and (c) promotion of dry cord care.[9] CHWs provided a basic package of neonatal care (including clean care kits) with advice to keep the cord clean and avoid application of harmful substances. Village health workers (VHWs) were trained by the CHWs to deliver the cord care intervention and make home visits for 7 days. In group (a), the VHW cleansed the cord as soon as possible after the birth (recommended within 6 hours of birth) and in group (b) once a day for 7 days. In group (c) VHWs only promoted cord care messages during home visits. CHWs visited the newborn infant as soon as possible after birth (preferably within 24 hours) and every few days and classified the degrees of severity of omphalitis.

There were approximately 10 000 infants in each group. Neonatal mortality (per 1000 live births) was statistically significantly lower in the single-cleansing group (22.5) than the dry cord care group (28.3; relative risk (RR) 0.80, CI 0.65–0.98), but not the multiple-cleansing group (26.6). However, there was a statistically significant reduction in the occurrence of severe cord infection in the multiple-cleansing group. Most infants received cord-cleansing within 24 hours. A sterile instrument was used to cut the cord in 93% of study infants and non-study applications to the cord were uncommon at the time of cord cutting (6%) and follow-up (3%). There is no obvious explanation as to why mortality was not decreased in the multiple-cleansing group especially in view of the significant reduction in omphalitis in the group.

A RCT in Sindh province, Pakistan[10] compared four groups of newborns delivered by traditional birth attendants (TBAs) (working under the supervision of CHWs) who provided families with clean care kits as follows: (a) 4% CHX applied to the cord by the TBA at birth and once daily by family members for up to 14 days along with soap (containing phenol and carbolic acid) and educational messages promoting hand washing; (b) soap and hand washing; (c) 4% CHX (no hand washing promotion); and (d) dry cord care.[10] The first application of CHX was done by the TBA after tying the cord. CHX was applied to the umbilical stump and the base of the stump was also cleansed with CHX and the skin around it. CHWs visited all the newborns on days 1, 3, 5, 7, and 28 to assess for signs of omphalitis (and grade severity) and other illnesses. Those with moderate to severe omphalitis were referred to the nearest government health facility.

There were 2150–2550 infants in each group who completed 28 days follow-up. Some 98% of care providers reported at least one and 63% at least three applications of CHX per day for a mean (SD) duration of 11.1 (2.8) days. There was a statistically significant reduction in omphalitis in infants who received CHX application (p=0.002). There was strong evidence of reduction in NNM in those who received CHX (42%, p=0.003) but no effect of hand-washing promotion or interaction between CHX and hand washing. There was no difference in time to separation of the cord between groups.

During the previous delivery only a quarter of the families used a clean delivery kit and 80–91% applied a home application to the cord which include an antiseptic in 9–20%. The substance most widely applied to the cord in Pakistan is 'surma' composed of ground lead. The local reaction to which may encourage invasion by pathogens. Other substances include ash, oil, and rarely cow dung. A limitation of the study was that hand washing practice could not be confirmed and it did not exclude other substances being applied to the cord.

The reduction in NNM demonstrated by the latter three studies [8–10] should prompt WHO to consider including CHX in clean delivery kits. However, the feasibility and sustainability of routine CHX application to the cord in government health services is a challenge.[11] It would depend on the degree to which TBAs and skilled delivery attendants were incorporated into the front line of the service. Application of CHX as soon as possible after birth to prevent other substances contaminating the cord would seem to be important. Whether single or multiple applications are required needs consideration. The latter would appear to be more logical. If families believe that CHX is beneficial there should be no problem in persuading them to undertake the application to the cord for up to 10 days or so.[11]

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Africa HEALTH CPD Challenge
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