BMJ

Treating severe malaria

Rectal artemether may be as good as intravenous quinine

Every year over a million children die of malaria in Africa. In many settings, especially rural ones, most fatalities due to malaria occur outside hospital, although a substantial proportion of these children will have made contact with some level of healthcare in their final illness.[1] Of those who arrive at hospital, many are moribund and up to half of malaria deaths in hospitals occur within 24 hours of admission.[2] Buying time by being able to start effective treatment for those with severe malaria in the community therefore has the potential to save many lives. Conventional treatment for severe malaria in Africa is intravenous or intramuscular quinine. Providing parenteral treatment with quinine in the community is usually impractical and potentially hazardous. Even in hospitals, staff are often overstretched and have some difficulty managing intravenous quinine safely.

In this issue Aceng et al report a randomised trial of intravenous quinine compared with rectal artemether in cerebral malaria.[3] They found that the effects of intravenous quinine and rectal artemether were comparable, both in terms of efficacy and time to recover. The rectal artemether group had a non-significant survival advantage. These are encouraging results. As Aceng et al acknowledge, a single trial of this size cannot alone be the basis for policy change. The current study would only be able to detect a relatively large mortality difference. The mortality in the quinine group was also on the high side compared with some other studies. With these caveats, taken with a similarly sized recently reported trial of rectal artesunate compared with quinine and descriptive studies of artemisinin suppositories, rectal artemisinins, especially if given in the periphery, might be one safe and effective way to reduce the risk of children dying before reaching hospital.[4-6] Rectal quinine could potentially be used in a similar way. A Cochrane review found no clear evidence of difference in outcome between rectal and parenteral quinine, although it noted that most trials are small and confidence intervals around outcomes in the meta-analysis are wide.[7]

Use of an artemisinin suppository rather than nothing for cases of suspected severe malaria as they are referred to hospital seems to be justified, and further convincing evidence of effectiveness will probably not become available as few would consider it ethical on current evidence to compare this to placebo. Community health workers and traditional healers can be trained to recognise symptoms of cerebral malaria and to administer suppositories. It would be possible to incorporate rectal antimalarial treatment while sick children are being transported to hospital into existing initiatives such as the "Integrated Management of Childhood Illness,"[8] although the cost effectiveness of this approach would need to be assessed.

That treatment in the community with an artemisinin suppository for presumed severe malaria could reduce mortality is encouraging, but it is not without potential hazards. Its use might reduce still further the chances of clinicians considering alternative diagnoses. Doctors already tend to treat almost all severe febrile disease as malaria despite evidence that many of those who go on to die have bacterial disease.[9 10] Many patients who are referred to hospital fail to arrive because of the multiple barriers to poor people accessing care, and the fact that their guardians believe that they have been treated might exacerbate that situation.[11] Artemisinin drugs should always be given with a second antimalarial, either in combination or sequentially. If treating patients with an artemisinin suppository without subsequently giving a second drug became common it could increase the risk resistance to artemisinin. These worries should not, however, detract from the fact that providing effective antimalarial treatment close to home to reduce delay has the potential to save many lives, and that artemisinin suppositories seem effective and can be used in severely ill patients in whom oral treatment is impossible and parenteral treatment impractical.

Whether artemisinins given by any route should be replacing quinine as the initial treatment of choice for severe malaria in Africa remains an open question. Little convincing evidence exists either way in African children.[12] On current evidence the difference in mortality between them, if it exists, is not likely to be large and probably only multicentre trials will have the power to answer this. The study by Aceng et al does, however, suggest that rectal artemether should be considered as an alternative to quinine for such trials in a setting where healthcare workers are already overwhelmed, as its ease of use may lead to initial treatment being given more quickly.[13]

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Total hip replacement and NICE

New guidelines need to address several areas of uncertainty

Around 150-200 different hip prostheses are available for use. Some require cement fixation, some are cementless, and each consists of an acetabular and a femoral component. The evolution of hip replacement led to alterations in design and materials, some of which proved disastrous (the 3M Capital implant is the best known failure).[1] Guidelines for the selection of implants for hip replacement were introduced in the United Kingdom by the National Institute for Clinical Excellence (NICE) in 2000.[2] Knowledge of the NICE guidelines is limited among both patients and clinicians, and a noteworthy number of surgeons in the United Kingdom are perhaps using prostheses that are not specified as suitable.[3] Although guidelines do not suspend individual clinical autonomy, many surgeons are left in a quandary as to whether they are open to litigation.

The NICE guidelines set a rate of revision for failure of 10% or less for a given prosthesis at 10 years, or performance compatible with that benchmark at three years. Prostheses unable to satisfy these requirements should be the subject of formal research or observational study if the implant is already in use.[2] Concerns have been raised that NICE guidelines may replace the Bolam test in a court of law,[4] supplanting the custom that a doctor is innocent of negligence if he or she has acted in accordance with a practice accepted as proper by a reasonable body of men skilled in that particular art.[5]

In the United States, the Food and Drug Administration authorises which hip prostheses may be used, allowing a wide range. The American Academy of Orthopaedic Surgeons says that most orthopaedic surgeons select the prosthesis based on the patient's needs, the surgeon's own preference and experience, and perhaps those of their colleagues or mentors (personal communication, Murphy TB, 2004). The academy provides a comprehensive booklet on osteoarthritis of the hip, which incorporates design of hip prosthesis, materials, fixation, and the outcomes and survivorship of the various bearing surfaces.[6] Kaiser Permanente, the largest non-profit healthcare plan in the United States, does not produce specific recommendations on the selection of prosthesis but has set up a total joint registry in 2001.

Registries act as a valuable source of information on individual prostheses, allowing informed decisions. The Swedish hip arthroplasty registry was established in 1979. Finland followed in 1980. The Danish hip registry is about to publish its 10 year results, and the Danish national association has informed us that, these results will influence surgeons' choice in the future and act as guidelines" (personal communication, Thomsen PB, 2004).

In Norway, the view is that the Charnley prosthesis is the only device with good long term follow up results in excess of 15 years, and until long term results are available, uncemented prostheses cannot be recommended for routine use.[7] In Holland and Germany, there are no specific guidelines, and selection of prosthesis is left to the surgeon. Representatives of both these countries have emphasised that the cost of prostheses will play an increasingly important part in future (personal communication, van Osterhout F, Puhl W, 2004). A joint registry was introduced in the United Kingdom in 2003.

In our department, three implants were identified that did not meet the NICE criteria. One was included in a multicentre international trial. For the others, we raised funds from charitable events and manufacturers to appoint a research assistant and set up an observational study. We obtained ethical approval and identified patients from the operating theatre database and invited them for review three years after their surgery. We obtained hip scores and did radiological evaluations to confirm that the components meet the three year minimum benchmark recommended by NICE.

A spirit of cooperation with NICE is probably the best way forward for doctors and law makers alike. NICE guidelines, however, have areas of uncertainty. These include a lack of specific information on the acetabular component in published guidelines; lack of clarity on hybrid variants—either in the form of cementless and cemented technology combined, or in relation to cup and stem from different manufacturers; and the place of generic copies of original designs. Moreover, NICE guidelines do not cover implants in