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The Network's NEWSLETTER Rx

Association for Rational Use of Medication in Pakistan

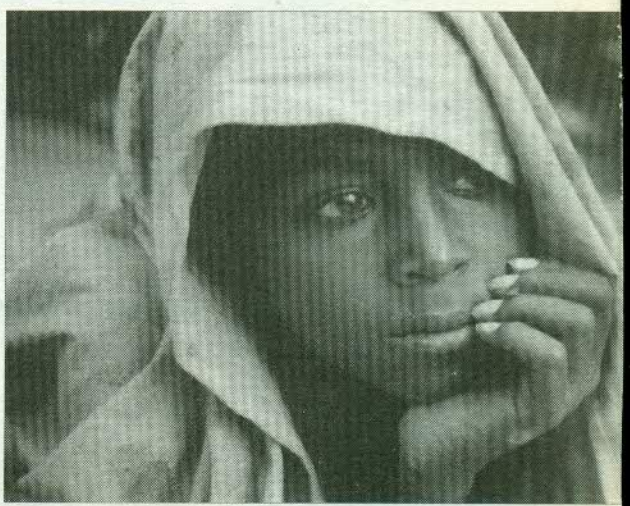
The Network s mission is to promote rational use of medication and essential drugs concept in Pakistan in order to optimize the usefulness of drugs and help bring equity in their access.

A policy paradox

The chances that a child will die before seeing his/her fifth birthday in Pakistan are seven times more than a child in a neighboring South Asian country, Sri Lanka. About half of these deaths are due to diarrheal diseases and acute respiratory infections.

These killer diseases are avoidable and can be successfully managed in earlier stages with very simple and effective measures. National Programs for Control for Diarrheal Disease (CDD) and Acute Respiratory Infections (ARIs) have clear protocols based on WHO guidelines for the management of children with these disorders. Both the programs recognize that the most important impeding factor in the "correct case management" of these disorders is unnecessary and incorrect use of drugs and the programs categorically condemn, as a policy, the use of anti-diarrheals and cough syrups.

It is ironical that in complete disregard to the policies of two most important Programs, the Drug Registration Board (DRB) of the Ministry of Health (MoH) keeps on allowing ever increasing number of anti-diarrheals and cough syrups to be available in the market. According to the results of our recent study (see page 10 for the preliminary report), currently more than 275 cough syrups and 65 anti-diarrheals are registered by the DRB. Majority of the cough syrups are combinations of up to seven active ingredients and some include chemicals like chloroform. Likewise, most of the anti-diarrheals are available in combinations and in pediatric formulations though adult formulations are also freely prescribed and given to children.



Both the programs and the DRB are run by the Federal MoH! This disturbing situation on the one hand clearly indicates obvious inconsistencies and gaps at policy levels of CDD - ARI and DRB and on the other hand provides evidence about the superficialness of government's efforts for "child survival".

We have initiated a process of dialogue at different levels involving all the stakeholders and sincerely hope that this clear demonstration of facts will lead to deregistration of unwanted drugs for diarrhea and ARIs and would also provide an opportunity to policy makers and members of the DRB to look into problems in registration procedures in general. These steps will strengthen our national programs and complement the efforts for child survival in the country.

NOTE

Due to shortage of space we cannot print details of references with each article. However, interested readers can get these references by sending a request to The Network. Please, mention the title of the article for which you need references and your complete postal address with the request.

Editor

▼Eclampsia: magnesium sulfate favored in anticonvulsant therapy

At least 500,000 women, overwhelmingly from developing countries, still die each year from causes related to pregnancy[1]. Eclampsia which now complicates only about 1 in 2,000 pregnancies in developed countries, but which is associated with a high mortality[2] is estimated to be a factor in about one in ten of these deaths[3,4] .

The pre-eclamptic syndrome of increasing blood pressure and proteinuria and its association with a risk of potentially fatal eclamptic convulsions during or immediately after pregnancy has been recognized by generations of clinicians. However, the cause of these remains obscure. Symptomatic anticonvulsant management of eclampsia with diazepam or phenytoin has been essentially empirical and based on the assumption that "eclampsia is a seizure like any other seizure"[5].

Parenteral administration of magnesium sulfate offers an alternative approach which has been widely practiced in the United States for the best part of a century[6,7]. Suggestions have been offered that it may exert a vasodilator or other effect that attenuates ischaemic brain damage[8-10]. However, lack of a proven, physiological-based therapeutic rationale for its action, and of any comparative assessment of its efficacy, has apparently frustrated its acceptance elsewhere[11]. Choice of treatment has been claimed to be more a matter of faith than of objectivity[12]. Clinicians have had to rely largely on experience conveyed in uncontrolled case series[6, 13-15], and on the outcome of a few small randomized trials[16-19], one of which decisively favored magnesium sulfate in a comparison with phenytoin[17].

Eclampsia now complicates few pregnancies in developed countries. However, it has proved possible to organize a multicenter randomized comparative trial of these two approaches to treatment on a scale required to provide statistically secure results in hospital centers in Africa, Asia and South America[20]. In these countries, eclampsia is still estimated to complicate as many as 1% of all deliveries[21-23].

The trial comprised two separate arms:

— diazepam was compared with magnesium sulfate in a sample of 910 women admitted to centers in Argentina, Brazil, Colombo, Ghana, India, Uganda, Venezuela and Zimbabwe; and

— phenytoin (administered after an initial loading dose of diazepam) was compared with magnesium sulfate in a sample 777 women admitted to four centers in India and South Africa.

Magnesium sulfate was administered as a slow intravenous loading injection of 4g (5g in South American centers) followed over the next 24 hours either by an intravenous infusion providing 1g/hour, or by an immediate intramuscular dose of 10g in divided dosage with a further 5g every 4 hours (as long as respiratory rate, knee jerks and urinary output raised no suspicion of over dosage). Whenever a further convulsion occurred, an additional 2-4g was given intravenously over 5 minutes.

Diazepam was administered as an intravenous loading dose of 10mg over 2 minutes, followed by two consecutive 24-hour intravenous infusions delivering 40 mg and 20 mg respectively.

Since phenytoin is recommended only for prevention of convulsions, patients allocated to this drug were pretreated with the intravenous loading dose of diazepam. This was followed by a loading dose of phenytoin, 1 g intravenously over 20 minutes (with continuous cardiac monitoring) followed by 100 mg every 6 hours for 24 hours.

The results obtained are interpreted by the collaborators as "providing compelling evidence in favor of magnesium sulfate, rather than diazepam or phenytoin, for the treatment of eclampsia." In both settings maternal mortality was lower among women allocated magnesium sulfate, but these differences did not attain significance. The case for favoring magnesium sulfate is based essentially on the finding that this intervention approximately halved the risk of recurrent convulsions when compared with diazepam, and reduced it by a somewhat greater margin when compared with diazepam/phenytoin.

Magnesium sulfate held no statistically demonstrable advantage over diazepam in