Correspondence

Call for Spontaneous Reports of Adverse Drug Events from Indian Physicians- Need of the Hour

Sir,

Adverse drug reactions (ADRs) are an inevitable consequence of drug use since few if any medications produce beneficial effects alone. These constitute a major health concern both for the individual patient and the community. It has been estimated that ADRs account for approximately 5% of all hospital admissions, occur during 10-20% of hospitalizations, and are responsible for 7-9% of hospitalization days. They also constitute a significant economic burden. The recent literature on risks associated with the use of Rosiglitazone (myocardial infarction) and Rimonabant (psychiatric side effects) highlights the tight rope walk for physicians who balance risks and benefits in an individual patient.

Worldwide, spontaneous reporting remains the cornerstone for capturing information on risks associated with medicine use. This simply put means that every physician should regard it as his or her duty and responsibility to report information on adverse reactions to the nearest ADR centre. What does one report? Ideally, all reactions. But most certainly serious, severe, unusual and unexpected reactions particularly with new drugs (those on the market for less than 4 years). One does not even need to establish a cause-effect relationship- a mere suspicion of an event (Adverse Drug Event or ADE) can be reported since causality (establishing a cause-effect relationship) can be done at a later stage using formalized algorithms and causality scales.

Where does one report this information? The National Pharmacovigilance program of India rolled out in November 2004 with support from the World Bank has established several centres around the country. Most centres have an approved one page form on their website that can be downloaded, filled and e mailed. For example, the ADR form of the South West zonal centre at the KEM Hospital, Mumbai is available on www.kem.edu/dept/clinical_pharmacology.htm. Functionally, information from peripheral centres is reported to the regional and from there to the zonal centres (Fig. 1). The zonal centres then send information to the office of the Drugs Controller General of India. Each centre also generates its own database and reporting can be done directly to any centre depending upon proximity.

The WHO defines Pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems. Clinical trials that are carried out in a few thousand patients are by default inadequate to answer questions on drug safety, since drugs are eventually used in a less well selected, much larger population. Indian physicians who treat a billion inhabitants are capable of generating a large volume of information on drug safety. While spontaneous reporting is mandatory in some countries, it is still voluntary in India. For India to be able to generate its own ADR database, it is imperative that physicians “spontaneously” begin reporting ADEs to the nearest pharmacovigilance centre to help generate our own ADE database.

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Several peripheral centres

Fig. 1
**Hypokalemic Paralysis Following Chikungunya Fever**

Sir,

Chikungunya fever is a viral disease, caused by Alphavirus, transmitted to humans by the bite of infected Aedes mosquitoes. Disease is characterized by an abrupt onset of fever, severe arthralgia, rash and other constitutional symptoms. Disease is usually self-limiting with fever lasting for 1-7 days. But sometimes disease may become morbid due to persistent joint pains, dehydration, electrolytes imbalance, hypoglycemia and neurological complications.

During the recent outbreak of Chikungunya fever in various parts of India, we came across a case of quadriaparesis with severe hypokalemia after an acute attack of Chikungunya fever.

A 26 years male was admitted with complaints of fever and joint pains predominantly involving knee and wrist from last 3 days. On examination patient was febrile (101 F), pulse - 90 min regular, blood pressure -110/70 mm Hg and normal general physical and systemic examination. There was no joint swelling or effusion and redness but movements of knee and wrist joint were painful. Laboratory investigations including complete haemogram, renal function test and liver function test were within normal limit. Chikungunya IgM antibody (by CTK, biotech card test) and CRP were positive. Serum Sodium - 136 meq/L, S. Potassium - 4.3 meq/L were within normal limit. Patient was treated symptomatically, improved and discharged after 2 days with mild joint pains.

Patient was readmitted after 7 days with complaints of sudden onset of weakness in all 4 limbs from last 6 hrs. There was no history of paresthesiae, trauma and diarrhea, vomiting, strenuous exercise followed by rest, intake of heavy carbohydrate diet and any drugs (diuretics) preceding the weakness. There was no history of such weakness in the past and no family history of episodic weakness. General physical examinations was normal. In CNS examination higher mental functions and cranial nerves were normal. Motor system examination showed normal muscle bulk and nutrition, hypotonia in all 4 limbs with power 1/5 in both upper limbs and 3/5 in both lower limbs with diminished deep tendon reflexes and flexor plantar response and no sensory deficit. Repeat investigations including complete hemogram, liver function tests, kidney function tests and thyroid profile (T<sub>3</sub>, T<sub>4</sub>, TSH) were within normal limits. S. Sodium was 143 meq/L whereas S. Potassium was only 1.9 meq/L. ECG showed flattening of T waves and presence of U waves. With the diagnosis of hypokalemic motor paralysis patient was treated with 40 meq KCL infusion in 5% 500 ml of dextrose drip. Patient improved remarkably within next 6 hrs with no neuro-deficit. Repeat S. Potassium was 5.4 meq/L and repeat ECG also revealed disappearance of U waves. Challenge test with heavy carbohydrates diet and strenuous exercise followed by rest, 7 days after the discharge did not produce any weakness.

Markedly low S. Potassium level (1.9 meq/L) with flaccid paralysis and complete recovery with Potassium infusion (40 meq/L) in this case confirms the diagnosis of hypokalemic paralysis. Other causes of hypokalemic paralysis are thyrotoxicosis and other conditions leading to hypokalemia such as urinary Potassium wasting syndrome (Bartter’s, Gitelman’s syndromes and acute tubular necrosis) alcohol, drugs (diuretics) and gastrointestinal losses. These were ruled out by clinical examination and relevant investigations. Familial periodic paralysis is unlikely because of following reasons :- (1) First episode of weakness. (2) Age more than 25 years. (3) Marked alteration in serum Electrolyte level. (4) Negative Challenge test.

Nerve conduction velocity to rule out G.B. Syndrome could not be done as patient was admitted in emergency hour. Marked hypokalemia and subsequent complete recovery with Potassium infusion also rules it out.

Hypokalemic paralysis can occur after a febrile illness. In this case, the febrile episode was Chikungunya fever about which comparatively less scientific information is available in the literature. The association, is interesting and needs to be shared.

**REFERENCES**