Letter to the Editor

Good Pharmacovigilance Practice: Accountability of Ayurvedic Pharmaceutical Companies

Sir,

There is a paucity of systematic documentation apropos the occurrence of adverse drug reactions (ADRs) and other safety issues of Ayurveda medicines. National Pharmacovigilance program (NPP) for Ayurvedic drugs is concerned with re-evaluation of marketed drugs, risk management, promoting rational drug use, and crisis preparedness. However, its successful implementation is a collective responsibility of the stakeholders viz. physicians, pharmacists, patients and pharmaceutical industry, that need to be sensitized towards reporting ADRs. This is a concern, especially in India, where there is below 1% reporting rate of ADRs as against the world rate of 5%.[1] In India, physicians are generally reluctant towards ADR reporting, due to poor awareness or lack of time/training.[2,3] Furthermore, poor knowledge, attitude and practices of Pharmacovigilance (PV) has been observed in Ayurvedic practitioners.[4-6] Till date, negligible number of ADRs to Ayurvedic medicines are reported/recorded in the NPP in India. This can be due to either the firm belief among practitioners that Ayurvedic drugs are safe or their lack of knowledge or awareness about the concept and significance of PV.[7] Marketing representatives (MRs) from Ayurvedic pharmaceutical companies approach physicians for the promotion of their drugs. While a new Ayurvedic drug [newly designed formula or new dosage form, which we treat as ‘New Chemical Entities’ (NCEs)] is promoted among physicians, it is important to discuss the reporting of ADRs. But, there is no data on whether such information is disseminated by MRs.

To explore this, we undertook a survey using a questionnaire (validated and consisted of four items), during July-October 2016, on 277 Ayurvedic physicians, selected using simple random sampling, working in rural and urban regions of Himachal Pradesh. We obtained their consent to participate and informed them that the participation is voluntary and confidentiality will be maintained. The questionnaire was communicated through WhatsApp to participants and they were asked to send it back to us with answers. The collected data were analyzed using MS Excel 2007 and expressed in percentage (%). General data on characteristics of 277 physicians is as follows:

Age group (years): 25-35 = 163 (59%), 35-45 = 67 (24%), >45 = 47 (17%);
Gender: Male = 192 (69%), Female = 85 (31%);
Professional qualification: graduates = 266 (96%), post-graduates = 11 (4%);
Working experience as physician: ≤5 years = 109 (39%), >5 years = 168 (61%);
Type of clinical posting: Posted in government Ayurvedic Health Centres (AHCs)/sub-divisional AHCs/district/state-level Ayurvedic hospitals = 103 (37%), Posted in mobile health units under NRHM = 43 (16%), Others (Pvt. practitioners/working in NGOs) = 131 (47%);
Average number of MRs met every week: 1-2 MRs = 269 (97%), 3-4 MRs = 8 (3%).

All the physicians reported that they have been approached by MRs for promotion of new products at least once. Only 1/277 (0.4%) physicians opined that they were given details regarding the need to report ADRs for their new product. None of the practitioners (0%) opined that they were informed by MRs for being vigilant in reporting ADRs for new products especially when used in vulnerable population (children, pregnant and lactating women, elderly). Additionally, 261/277 (94.2%) participants revealed that MRs informed about the systematic evaluation and safety details of their new products to them. But, none (0%) received ADR reporting form by the MRs.

The study found a very poor intimation of reporting ADRs of new Ayurvedic products by MRs to prescribing physicians. This reflects a lack of sufficient efforts of pharmaceutical companies towards PV. Studies suggest that MRs on behalf of the pharmaceutical companies try to influence the prescribers, provide information often biased towards the promoted product, offer gifts, services, and flattery to physicians to request favors, in the form of prescriptions.[8-11] and physicians generally fail to recognize the inaccurate statements.[9] Moreover, the quality of information provided by MRs to physicians on risk, harmful effects, and contraindications of their promoted drugs is often low.[12] All such factors may lead to misrepresentation of the actual therapeutic value of the medicines and ignorance of safety issues.

Apart from classical Ayurvedic formulations, another category of Ayurvedic medicines available in market are patented proprietary formulations made of herbal extracts.[13] Pharmaceutical companies generally strive to develop new dosage forms from classical formulations or pick few formulations from literature, make slight changes in ingredients or ratio, and market them as newly “designed” formulae under new brand names and
claim it to be wonder medicines. The changed formulae or new dosage form is no longer a classical drug and hence has unproven or dubious pharmacokinetics and pharmacodynamics. These must be treated as NCEs. Each herb/mineral component of new “designed” formula is an independent moiety with distinct molecular targets; they may act antagonistic or have unknown mechanisms or effects (short/long-term). Most of the pharmaceutical companies generally set their own therapeutic claims based on individual components of new formula or new dosage forms, neglecting scientific validations such as: pre-clinical/ clinical screening, drug interactions (drug-drug/drug-food), stability, bioavailability, safety studies (short/long-term), dose determination etc., which may lead to adverse events, setting the human lives in jeopardy.

Commercialization of Ayurvedic medicines has brought many serious challenges in pharmaceutical sector that need to be addressed, such as: Inadequate regulatory measures, weak quality control systems, spurious and counterfeit drugs, non-compliance of classical guidelines especially for herbo-mineral and medicines that include drugs of Schedule E-1, uncontrolled distribution channels (including mail order, internet sales or sales over the counter), pitiable clinical evaluation (poorly designed, sporadic, uncontrolled, unregistered in CTRI) of marketed products, violation of laws against objectionable advertisements act, false/incomplete information apropo drug to physicians, poor market surveillance/feedback, under-reporting or poor Periodic Update Safety Reporting (PSUR), biased approach for drug promotion, tie-ups with physicians, etc., Sometimes pharmaceutical companies overlook reporting fearing that the acknowledgement of ADRs may reflect negatively on their competence, market goodwill, or put them at risk of litigation. In order to safeguard patients, all such flaws should be dealt with stringent legislations.

As a recommendation, the authors suggests: (i) Prompt ADR reporting by manufacturers to regulatory authorities that should become as a part of their regulatory framework; (ii) Aggregate reporting, in the form of PSUR’s (in Schedule Y or ICH E2C format) for drug safety and risk-benefit evaluation should be encouraged, to get a broader view of the safety profile of a drug; (iii) Marketing authorization holder should be made accountable for continuous safety monitoring of new medicines; (iv) Pharmaceutical companies must conduct a comprehensive drug safety and PV audit to assess their compliance with worldwide laws, regulations, and guidance; (v) MRs should be trained on importance of PV and the need to convey the same to the prescribers when a new Ayurvedic medicine is being promoted. The inherent uncertainty of the risks and benefits of drugs needs to be acknowledged and explained.

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Conflicts of interest
There are no conflicts of interest.

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