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Injectable diclofenac: A painful shot into Iran's health system

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Abstract

Despite high accessibility to medicines, irrational prescribing of injections is a characteristic of Iran's health system and it has been reported that more than 40% of patients who visited a doctor receive at least one injection. The injectable dosage form of Diclofenac was introduced into the Iran drug market in 1993. However, its use rapidly increased shortly post commercialization and its sale increased to 85,520,000 ampoules in 1998. Not unexpectedly, the Iran pharmacovigilance center received a substantial number of reports indicating adverse drug reactions (ADR) following the use of injections and specifically with that of Diclofenac injection. A total number of 176 ADR citing major problems following intramuscular administration of Diclofenac were reported to Iran's pharmacovigilance center in the period of 1996–2002. Although a multi interventional policy including educational, regulatory and managerial interventions was able to bring ADR due to Diclofenac injection under control, statistics shows that prescribers are now trying to substitute Diclofenac injection by other injectable medicines.

Keywords: Irrational drug use; Injections; Pharmacovigilance; Diclofenac injection; Iran

Introduction

Since Alexander Wood introduced the use of a hollow needle for direct injection of opioids to treat neuralgia (Brokensha, 1999), this practice has become increasingly popular both in developed and developing countries. However, nowadays overuse of injections is only a common characteristic of health systems in developing countries (Hutin, Hauri, & Armstrong, 2003). Not only are vast numbers of injections unnecessary and unsafe but they have also been linked to the possible transmission of millions of cases of viral hepatitis B and C and significant cases of HIV infections (Kane, Lioyd, Zaffran, Simonsen, & Kane, 1999). In different cultures of developing countries the belief in injections as a very powerful method of restoring or maintaining health is shared by health professionals and lay people alike (Bhattarai & Wittet, 2000). Despite the fact that injections are overused in developing countries, there is still not a concrete response to the basic question of why injections are so popular in these countries. The abuse of injections also has economic consequences and health systems have to pay for this unnecessarily expensive form of medicine administration in spite the fact that oral dosage forms would be more appropriate and carry less risk to the patients (Reeler, 2000).

Iran is a country of 67 million populations with a fairly advanced health system. Despite improvement

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of availability and affordability of medicines in Iran there is convincing data that prescribing of medicines is excessive (Cheraghali et al., 2004). It has been reported that more than 40% of patients who visited a doctor received at least one injection (Cheraghali 2003). Iran pharmacovigilance center in period of 1997–2002 received substantial number of reports indicating adverse drug reaction (ADR) following use of Diclofenac injection. In this paper problems affecting the Iran's health system and patients from administration of unnecessary Diclofenac injection and interventions used to overcome the problem have been explained.

Interventions

Diclofenac is a commonly used non-steroidal anti-inflammatory medicine and is being used to treat pain and inflammation. The injectable dosage form of Diclofenac was introduced into Iran drug market in 1993 through local production and marketed by its International Nonproprietary Name (Diclofenac). However, its use skyrocketed (Annual Reports, 1996–2003) and appeared in most of prescription written by general practitioners and according to statistics published by a centralized data collection center in Ministry of Health (MOH), attained a peak usage of 85,520,000 prescriptions in 1998 (Fig. 1). The center regularly collects data from producers, importers, wholesalers and distributors of medicines in Iran. Iran pharmacovigilance center has received the first ADR reports following administration of Diclofenac injection in late 1996. However the increasing number of reports was alarming and the center confirmed that the medicine was a contributory factor to the adverse reactions reported. Number of ADR reports reached a record high of 69 reports in 1998. Despite the fact that Iran pharmacovigilance center was newly established and number of prescribers reporting to the center were limited, a total number of 176 ADR reports indicating major problems following intramuscular administration of Diclofenac were reported to the center during the period of 1996–2003 (Table 1). Following receipt of these reports Iran ADR center through its communication with WHO center and other pharmacovigilance databases realized that such side effects had not been reported elsewhere (or at least not recorded) as side effect of Diclofenac injection.

In 1997, the pharmacovigilance center launched a massive educational campaign, including educational workshops on rational use of injectables for physicians and using both public media and medical journals in order to warn against serious side effects of Diclofenac injection and to emphasis that prescribers should not prescribe Diclofenac injection for common illness treated in out patients. The "Dear Health-Care Professional" letters also explained that Diclofenac injection was not indicated to treat common conditions such as fever in adolescent younger than 13 years old. One year after the intervention, use of Diclofenac injection substantially decreased although still remained above a justified value (Fig. 1). However, due to continual reports of ADR and in an attempt to find out the cause, national quality control labs become involved. Although registration is a pre requisite for

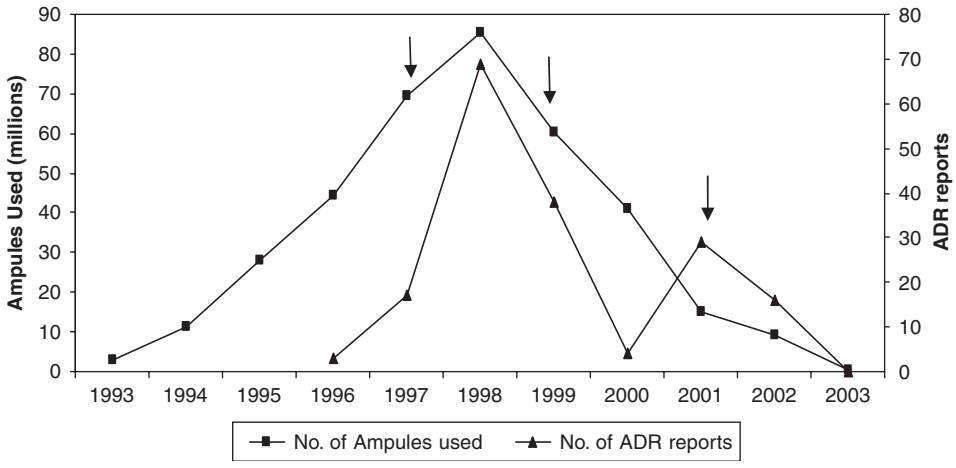

Fig. 1. Trend of use of Diclofenac injection and number of ADR reports 1993–2003. Arrows show time of interventions. First intervention (1997) educational campaign, 2nd intervention (1999) and 3rd intervention (2001) restriction on use of the medicine.

Table 1
Reported ADRs following intramuscular injection of Diclofenac to Iran pharmacovigilance center 1996–2003 according to type of adverse effects and patient's gender. In some patients more than one side effect reported

Year	No. of ampoules used (millions)	Foot drop	Leg paralysis	Walking difficulty	Total	Gender	
						F	M
1996	44.4	1	0	2	3	1	2
1997	69.3	6	6	5	17	7	11
1998	85.5	33	16	20	69	16	38
1999	60.5	9	12	17	38	14	26
2000	41.4	1	2	1	4	1	3
2001	15.1	13	4	12	29	14	15
2002	9.3	10	0	6	16	5	11
2003	0.4	0	0	0	0	0	0
Total	325.6	73	40	63	176	58	105

marketing of any locally produced or imported medicines in Iran, it was necessary to investigate the possibility of any inconsistencies in quality of Diclofenac injection marketed in Iran. Diclofenac injections in Iran drug market were produced by seven different pharmaceutical companies. Meticulous and lengthy evaluation of the starting material and final formulation of the products in the market using sophisticated lab techniques by national quality control labs revealed that all of Diclofenac injections met standards cited in international pharmacopoeias. Despite this, the MOH in a precautionary measure decided to temporarily stop local production of Diclofenac injection and imported the original brand of Diclofenac injection, Voltaren. However, careful follow up of Voltaren use also revealed the incidence of same type of adverse effects following intramuscular administration. This fact proved that the adverse effects were due to the Diclofenac injection itself, although the cause was still unknown. Although during all of these activities the pharmacovigilance center still aggressively continued its educational intervention, there was evidence that this intervention was not as effective as it was expected and the center continued to receive reports of severe adverse reaction from Diclofenac injection (Fig. 1). However, the total number of ADR reports was reduced from 69 in 1998 to 38 in 1999.

At this stage the MOH issued a regulatory alert to the prescribers warning that patients affected by side effects of Diclofenac injection prescribed for an unjustified condition might sue prescribers in a court claiming for compensations for damages from avoidable side effect of the drug. In fact this happened and several patients filed such suits against prescribers. This intervention was also substantially reduced use of Diclofenac injection (Fig. 1).

In the final intervention to prevent severe walking difficulties including sciatic nerve damage and permanent paralysis following injection of Diclofenac, the MOH announced a policy to restrict the prescribing of Diclofenac injection and to limit distribution of the medicine only to hospitals and clinics. At this time the MOH banned prescribing of Diclofenac injection for out patient conditions. Since pharmaceuticals distributors were also under regulation of MOH, the national regulatory authority was able to implement its decision. This intervention effectively reduced use of Diclofenac injection to a low level of less than 400,000 injections in 2003. Along with this, number of reported ADRs due to injection of Diclofenac has reduced from 29 in 2001 to 16 in 2002 and zero in 2003.

Discussion

Evidences of irrational use of drugs including high number of drugs per prescription, high use of injectable and antibiotics are present in Iranian prescibers' behavior (Cheraghali et al., 2004). Unnecessary injections in Iran most often include administration of vitamins and painkillers. Despite the fact that nearly all providers have high awareness of the risks associated with injections, at least in half of the cases, a patient's treatment in Iran

basically consists of the administering at least one injection. There is a general perception that availability of an injectable pain killer even for out patient care is a "must" (Cheraghali, 2003).

The Iran health system in last decade faced a dreadful experience due to over use of Diclofenac injection in medically unjustifiable condition. A total number of 176 ADR reports which described walking difficulties following intramuscular injection of Diclofenac were reported to Iran pharmacovigilance center in 1996–2002. Consistency of the reports and their validity along with the fact that in most of the cases Diclofenac injection was both prescribed by qualified provider and administered by trained medical personnel dismissed the possibility of wrong injection technique as a contributory factor in adverse effects reported. Besides no reports of such adverse effects was reported by injection of other medicines (e.g. vitamins and antibiotics) in those centers reporting ADRs from Diclofenac injection.

Since it has been reported that educational, managerial and regulatory interventions could have substantial effect in improving use of medicines in developing countries (Laing, Hogerzeil, & Ross-Degnan, 2001), the MOH launched a multi interventional policy to tackle the problem. Along with issuing 9 alerting letters, regulatory and managerial interventions have been used to control the problem. Results of this multi interventional policy showed that in this case educational intervention was not sufficiently effective to overcome the inappropriate use of medicines.

Conclusion

Although providers commonly emphasis patients' demand as a major driver of injection overuse, surveys indicate that patients are open to alternatives to injections. Prescribers overestimate patients' preference for injections and have false preconceptions about their effectiveness (Bhattarai & Wittet, 2000). Experience has shown that isolated interventions aimed at specific aspects of people's behavior often fail to meet their objectives. Therefore a combination of educational, managerial and regulatory interventions has been proposed to combat prescribing problems. Despite the fact that prescribers tried to limit prescription of Diclofenac injection following educational interventions, some physicians attending educational workshops on rational use of injectables repeatedly asked for an alternative injectable painkiller. Although these combined interventions was able to bring adverse drug reactions due to Diclofenac injection under control and reduced the number of Diclofenac injection used in Iran in 2003 to a record low of less than 400,000 injections, unfortunately it seems that attitude of prescribers toward injections did not change and statistics published by MOH shows that prescription of other injectables such as corticosteroids or Tramadol has been increased (Annual Reports, 1996–2003). It may be concluded that prescribers are trying to substitute Diclofenac injection by other inejctable medicines. This is in line with previously published results emphasizing the role of prescribers on irrational use of injectables (Cheraghali et al., 2006). This indicates that health policy makers should develop and implement comprehensive interventions to rationalize prescription of injectable medicines.

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References

Annual Reports. (1996–2003). *Department of pharmaceutical affairs*. Iran: Iran Ministry of Health.

Bhattarai, M. D., & Wittet, S. (2000). *Perceptions about injections and private sector injection practices in central Nepal*. General Welfare Pratisthan Gates Children's Vaccine Program at PATH, pp. 1–35.

Brokensha, G. (1999). The hollow needle: Inappropriate injection in practice. *Australian Prescriber*, *22*, 145–147.

Cheraghali, A. M. (2003). "Rational drug use" promoting activities in Iran: A successful trend. *Essential Drug Monitor*, *33*, 10–11.

Cheraghali, A. M., Nikfar, S., Behmanesh, Y., Rahimi, V., Habibipour, F., Tirdad, R., et al. (2004). Evaluation of availability, accessibility and prescribing pattern of medicines in the Islamic Republic of Iran. *Eastern Mediterranean Health Journal*, *10*, 1–10.

Cheraghali, A. M., Solemani, F., Behmanesh, Y., Habibipour, F., Ismaeilzadeh, A., Nikfar, S., et al. (2006). Physicians' attitude toward injectable medicines. *Journal of Pharmacology and Toxicology*, *1*, 33–39.

Hutin, V. J., Hauri, A., & Armstrong, G. L. (2003). Use of injections in healthcare settings worldwide, 2000: Literature review and regional estimates. *British Medical Journal*, *327*, 1–5.

Kane, A., Lioyd, J., Zaffran, M., Simonsen, L., & Kane, M. (1999). Transmission of hepatitis B, hepatitis C and human immunodeficiency viruses through unsafe injections in the developing world: Model-based regional estimates. *Eastern Mediterranean Health Journal*, *77*, 801–807.

Laing, R. O., Hogerzeil, H. V., & Ross-Degnan, D. (2001). Ten recommendations to improve use of medicines in developing countries. *Health Policy Planing*, *16*, 13–20.

Reeler, A. V. (2000). Anthropological perspectives on injections: A review. *Bulletin of World Health Organization*, *78*, 136–143.