Original Article

Steroid Contamination in Drugs Pak Armed Forces Med J 2012; 62 (3): 361-4

FREQUENCY OF STEROID CONTAMINATION IN DRUGS PRESCRIBED BY QUACKS IN RAWALPINDI

Syed Tanveer Abbas Gilani, Dilshad Ahmed Khan, Mushtaq Ahmed, Farooq Ahmad Khan

Armed Forces Institute of Pathology Rawalpindi

ABSTRACT

Objective: To determine the frequency of contamination of steroids in drugs prescribed by quacks, being used by patients in Rawalpindi.

Study Design: Cross- sectional study.

Place and duration of study: Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology Rawalpindi, from June 2010 to March 2011.

Patients and Methods: One hundred and seventy eight drugs distributed by quacks in Rawalpindi were collected from the patients. Quackery formulations (QF) were analyzed by thin layer chromatography on fluorescent Aluminum silica plates by using mobile phase of methylene chloride: ether: methanol: water (77:15:8:1.2) and relative flow of spots were noted. Samples positive for steroids were confirmed by high performance liquid chromatography.

Results: Out of In total of 178 samples, 125 (70.2%) were received by patients from unregistered hakeems, 29 (16.3%) unregistered homeopaths and 24 (13%) directly from nonmedical shopkeepers, prescribed for in joint pains 84 (47%), generalized weakness 43 (24%), dermatitis 28 (16%), gastrointestinal diseases 12 (7%) and respiratory diseases 11 (6%). Out of 178 samples, 38 (21%) QF were contaminated with steroids found in 18 (48%) tablets, 10 (26%) powders, 5 (13%) creams, 3 (8%) capsules and 2 (5%) syrups. Out of 38 Steroid contaminated QFs 20 (53%) countrained dexamethasone, 12 (32%) prednisolone, 4 (10%) hydrocortisone and 2 (5%) betamethasone.

Conclusion: In modern era, patients are still using drugs prescribed by quacks and 21% of QF in Rawalpindi is contaminated with steroids. The steroids comprise mainly of dexamethasone and prednisolone in adulterated tablets and powders prescribed by hakeems.

Keywords: Quacks, Quackery formulations, Steroids, Thin layer chromatography.

INTRODUCTION

In our country some of the patients are still using drugs prescribed by quacks for different diseases. These drug formulations are prepared by mixing different drug without formal medical education and knowledge, labeled as Quackery formulations (QF)[1]. These uncertified QF mixtures are dispensed by unregistered hakeems, homeopaths and shopkeepers directly in the form of tablet, capsule, powder, liquids, raw materials such as tea or concentrated extracts and applied as a paste on the skin[1,2]. People in developing countries take them because of the cultural beliefs, lowwest, easy availability and publicity by the quacks1. QF are the predominant form of health care in many underdeveloped populations[2]. Apart from the widespread usage of QF, there is a constant worry that some of QF available in the market may contain contaminants such as steroids[3].

Many quacks contaminate drugs with steroids for early relief of symptoms, although they do not label their formulations or indicate the steroid content. Excessive dose and long-term usage of medications contaminated with steroids, weaken the immune response and reduce the ability to fight against infections, increase blood pressure, acne, bruising, swollen hand, stomach upset, muscle weakness or joint pain, increased hair growth and osteoporosis[2,4].

According to WHO reports, across the world, 10-30% of pharmaceuticals are counterfeit or adulterated, 15 to 20% of the medicines sold in India are adulterated and in China 13.1% of the 20,000 samples tested were either adulterated or substandard[5,6]. National regulatory conference 2008 adulteration screening results of enforcement samples showed that 13.3% were positive for steroids[7].

Correspondence: Brig Dilshad Ahmed Khan, Dept of Chemical Pathology, AFIP Rawalpindi
Email: dakhan@cpsp.edu.pk
Received: 11 May 2011; Accepted: 06 Oct 2011

A Malaysian study showed that out of 102 analyzed samples, 27.5% were positive for prednisolone, 34.3% positive for unknown steroids and 38.2% were negative for both steroids[1]. Taiwan survey showed that out of 2,609 herbal formulae analyzed, 23.7% were contaminated with pharmaceutical adulterants and a study of 243 proprietary products in California found that 7% contained undeclared pharmaceuticals, most commonly caffeine, paracetamol, indomethacin, hydrochlorothiazide, and prednisolone[2]. Studies have shown that 70% of patients who use QF do not inform their treating physicians[2].

In Pakistan a major proportion of population is un-educated and there is a lack of proper medical care facilities even in the cities for poor patients. These people take the QF from different sources. Because of the lack of comprehensive regulations regarding quackery practice and standards for QF, it is imperative that these drugs be screened for steroids with an aim to protect the patients from adverse effects of these contaminants[8,9]. The objective of our study was to determine the frequency of contamination of steroids in drugs prescribed by quacks in Rawalpindi.

PATIENTS AND METHODS

A cross-sectional study was conducted at the Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology (AFIP) Rawalpindi, Pakistan from Jun 2010 to March 2011 after approval of the institutional review committee. One seventy eight QF used by the patients were randomly included from Rawalpindi after informed consent. All those drugs whose constituents are known to have steroids and allopathic medicines were excluded.

Total 178 QF prescribed by quacks, whose constituents were unknown to have steroids, self prescription, unlabelled drugs, uncertified mixtures of unregistered hakeems, homeopaths and herbal products, used by either sex of any age were included in the study. These QF were willingly given to the researchers and were kept in the cabinets or refrigerator for analysis at a later date. History was taken from the patients and drug samples were collected which were in the form of pills, tablets, capsules, powder, creams, syrups, raw materials and tea. Samples were mechanically crushed, extracted or cleaned up to remove undesired impurities. Extraction of the 1g or 1ml sample was done with 4 ml of ethanol in plain tubes. Samples were centrifuged for 5 min at 1,000 g[10].

Analysis of steroids

The supernatant layers of the extracted samples were spotted on TLC plate manually by jet capillary tube, with 6 samples at a time to save time and cost. Standards of the dexamethasone, prednisolone, hydrocortisone and betamethasone were also applied along with samples. We used aluminum plates with silica layer of 250µm in thickness (fluorescent) as stationary phase. The chromatograms were developed by putting the plates into a glass TLC development tank containing mobile phase consisting of Methylene chloride: Ether: Methanol: Water as 77:15:8:1.2 respectively. Chromatograms were developed to 7-10 cm from the origin. The substances were separated by elution with the mobile phase on these plates. After drying the plates, were exmined under UV lamp (254 nm), and fluorescent spots were seen in samples positive for steroids or were saprayed the plates with 20% sulfuric acid in ethanol followed by heating at 105^0C for 10 min and detection of colored spots[11,12].

Diagnostic criteria was to calculate the relative flow (Rf) value of the spots detected and to compare it with the standard Rf values of the steroids applied or with given table of book of Clarke's analysis of drugs and poisons[8,9]. Samples positive for steroids were confirmed by high performance liquid chromatography (HPLC)[13]. HPLC was performed with C 18 column with a gradient mobile phase of water and acetonitrile. Detection was with diod array detector[14,15].

Statistical analysis of all the data was entered in statistical package for social sciences version 17 (SPSS Inc, Chicago, IL, USA). Mean, SD and ranges were calculated for quantitative variables like age and duration of drug use. Frequencies and percentages were calculated

for qualitative variables like gender, source, indications, types of QF, steroids contamination and type of steroids detected.

RESULTS

A total of 178 QF were provided by the patients comprising 110 (62%) males and 68 (38%) females with mean age of 44, ranging from 12 to 75 years. The duration of use of QF by the patients ranged from 1 to 28 weeks with mean duration of 6 weeks. The patients were taking different types of QF from unregistered hakeems, homeopaths and directly from nonmedical shopkeepers as shown in the Table.

Most of the patients (47%) were using these medication for joint pains, generalized weakness (24%), dermatitis (16%), gastrointestinal diseases (7%) and respiratory diseases (6%). The QF was prepared in different formulation and mainly dispensed as powders (31%), tablets (27%), syrups (20%), creams (13%) and capsules (9%). The frequency of steroid positive preparations is shown in Figure-1.

Out of 178 QF collected from the patients, 38 (21%) samples were found positive for steroid contamination and 140 (79%) samples were negative for steroids. The types of steroid are shown in Figure-2.

DISCUSSION

The QF was an alternative treatment to the patients to cure their diseases. QF are cheaper and available in every shop easily and through friends in different areas. Also, some of the patients may be attracted by the sellers who claim that their drugs do miracle to cure diseases. Our study showed that many patients were using QF in this modern era. More than 60% Asians use herbal medicines for health or treatment of various diseases[5]. Use of QF was found higher in males as compared to females as they have more opportunities to visit quacks. Majority of middle aged patients were taking different QF for an average period of 6 weeks, showed that QF were an important aspect of their lives for long term use. Excessive dose and long-term usage of medications that are contaminated with steroids may lead to many adverse effects[1,2,4]. Although steroids are prescribed by allopathic physicians for joint pains, dermatitis and chronic obstructive airway diseases but their doses are well

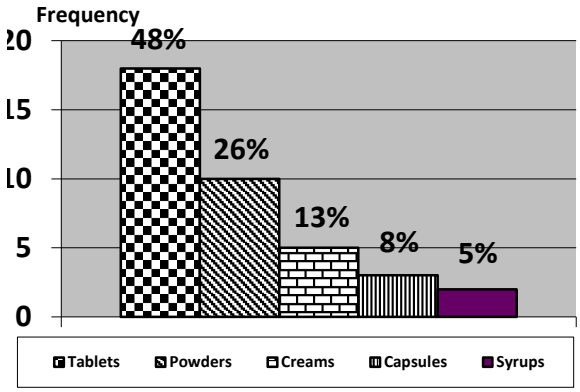

Fig. 1: Types of quackery formulations that were found positive for steroids, used by patients in Rawalpindi (n=38).

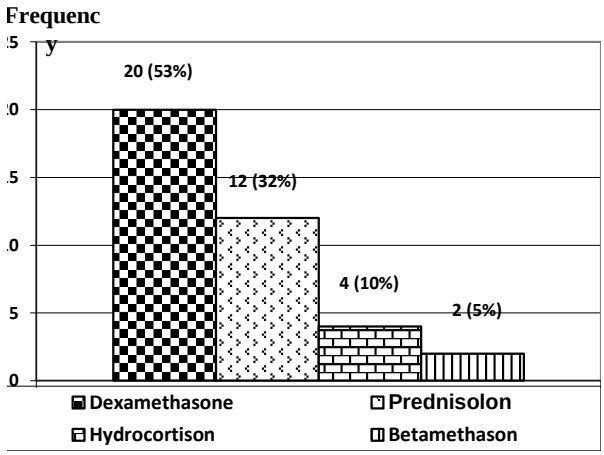

Fig. 2: Different types of positive steroids detected in quackery formulations in Rawalpindi (n=38).

Table: Baseline characteristics of patients who received drugs from quacks in Rawalpindi n (178).

Parameters	N (%)
Gender	
Male	110 (62%)
Female	68 (38%)
Steroids detection	
Positive	38 (21%)
Negative	140 (79%)
Sources	
Hakeems	125 (70.2%)
Homeopaths	29 (16.3%)
Non medical shopkeepers	24 (14.5%)
Indications	
Joint pains	84 (47%)
Generalized weakness	43 (24%)
Dermatitis	28 (16%)
GIT diseases	12 (7%)
Respiratory diseases	11(6%)

monitored to avoid side effects. The trends of utilization of QF in the form of powders, tablets and syrups were higher than creams and capsules. Polypharmacy was common in these patients[16]. The contamination of steroids were found higher in tablets and powders than other QF.

Steroid analyses of the QF collected from the patients in Rawalpindi showed steroids contamination in about 21 % of prescriptions. According to WHO reports, across the world, 10-30 % of pharmaceuticals were counterfeit or adulterated, 15 to 20% of the medicines sold in India were adulterated and in China 14.1% of the 20,000 samples tested were either adulterated or substandard[5,6]. A survey in Taiwan showed that out of 2,609 herbal formulae analyzed, 23.7% were contaminated with pharmaceutical adulterants[2]. National regulatory conference 2008 adulteration screening results of enforcement samples showed 14.3% positive for steroids[7]. In our study out of 38 QF that were contaminated with steroids, dexamethasone was found in 53 %, 32% prednisolone, 10% hydrocortisone and 5% betamethasone. A study on Malaysians showed that out of 102 analyzed samples, 27.5% were positive for Prednisolone, 34.3% positive for unknown steroids and 38.2% were negative for both steroids[1]. A study of 243 proprietary products in California found that 7% contained undeclared pharmaceuticals, most commonly caffeine, paracetamol, indomethacin, hydrochlorothiazide, and prednisolone[2]. Steroids have many side effects, which are detrimental to the health of the patients[17,18].

Our study showed higher rates of contamination of steroids as compared to other studies in literature.

Limitation of the study was that the QF were only qualitatively screened for detection of steroids, exact amount of steroids were not quantitated. Further studies are required to know and compare the frequency of steroid contamination in drugs prescribed in different areas of Pakistan and steroid levels in the blood of patients using QF positive for steroids and to find the adverse effects of steroids.

CONCLUSION

Patients in Rawalpindi are still using drugs prescribed by quacks and 21% of QF are contaminated with steroids in Rawalpindi. The steroids mainly comprising of dexamethasone and prednisolone were adulterated in the tablets and powders mostly prescribed by hakeems. So quackery formulations may be avoided or screened for steroids before use to avoid toxicity.

REFERENCES

1. Ismail Z, Mohamed R, Hassan MHM, Su KW. Usage of traditional medicines among elderly and the prevalence of prednisolone contamination. Malaysian Journal of Medical Sciences 2005; 12: 50-5.
2. Phua DH, Zosel A, Heard K. Dietary supplements and herbal medicine toxicities—when to anticipate them and how to manage them. Int J Emerg Med 2009; 2: 69–76.
3. Farooqui OA, Hosein T, Hosein MM. Addition of steroids in medicated Dentrifices marketed in Pakistan: A Possible serious health hazard. J Pak Med Assoc 2003; 53: 332-5.
4. Krishnaprasad R, Pillay VV, Rajesh RR, Vishnupriya N. Adulteration and contamination of Ayurvedic herbal medications. Journal of the Indian Society of Toxicology 2005; 1: 1.
5. Caudron JM, Ford N, Henkens M, Mace C, Kiddle-Monroe R, Pine J. Substandard medicines in resource-poor settings: a problem that can no longer be ignored. Tropical Medicine and International Health 2008; 14: 1062–72.
6. Newton P, Green M, Fernandez F, Day N, White N. Counterfeit anti-infective drugs. The Lancet Infectious Diseases 2006; 6: 602-14.
7. Muhammad MB. Techniques in identification of common adulterant in traditional medicines product. National Pharmaceutical Control Bureau (NPCB), National Regulatory Conference 2008.
8. Attarde DL, Aurangabadkar VM, Belsare DP, Pal SC. Report: quantitative estimation of beta-sitosterol, lupeol, quercetin and quercetin glycosides from leaflets of Soymida febrifuga using HPTLC technique. Pak J Pharm Sci. 2008; 21: 316-9.
9. Cieślaa L, Waksmundzka-Hajnos M. Two-dimensional thin-layer chromatography in the analysis of secondary plant metabolites. Journal of Chromatography A 2009; 1216: 1035-52.
10. Macherey-Nagel (MN) manual, Chromatography, Second Edition, 2000.
11. Flanagan RJ. Basic Analytical Toxicology, World Health Organization (WHO), Geneva 1995.
12. Bhawani SA, Sulaiman O, Hashim R and Mohamad-Ibrahim MN. Thin-Layer Chromatographic Analysis of Steroids: A Review. Trop J Pharm Res 2010; 9: 301-14.
13. Thevis M, Geyer H, Mareck U, Schänzer W. Screening for unknown synthetic steroids in human urine by liquid chromatography-tandem mass spectrometry. J Mass Spectrom 2005; 40: 955-62.
14. Park SJ, Kim YJ, Pyo HS and Park J. Analysis of corticosteroids in urine by HPLC and thermospray LC/MS. J Anal Toxicol 1990; 14: 102-8.
15. Mazzarino M, Turi S, Botrè F. A screening method for the detection of synthetic glucocorticosteroids in human urine by liquid chromatography-mass spectrometry based on class-characteristic fragmentation pathways. Anal Bioanal Chem 2008; 390: 1489-402.
16. Fillit HM, Futterman R, Orland BI, et al. Polypharmacy management in Medicare managed care: changes in prescribing by primary care physicians resulting from a program promoting medication reviews. Am J Manag. Care 1999; 5: 587-94.
17. Susan C. Smolinske, PharmD, DABAT. Herbal Product Contamination and Toxicity. Journal of Pharmacy Practice 2005; 3: 188-208.
18. Niggemann B, Gr_ber C. Side-effects of complementary and alternative medicine. Allergy 2003; 58: 707-16.