REVIEW ARTICLE

History of Neurological Disorders in Persian Medicine

Abstract

Many studies concerning Persian history have been performed. Persian physicians and scientists greatly contributed to medical sciences by their own observations, experimentations and skills through more than seven thousand years of Persian history. In Persian medieval medicine, different fields were described. Among these fields, neurological disorders, especially headache and epilepsy were explained in details. Medieval Persian physicians described the treatment of headache using many substances with different modes of actions. They attributed the therapeutic actions of plants to a specific analgesic, sedative or prophylactic drug property of variable strength. They also defined the epilepsy as a manifestation which begins suddenly, although premonitory symptoms, such as weakness, epigastric pressure or pain, depression, tongue paresthesia, spreading extremities paresthesia, sudden shock, incoherent speech, nightmare and sandness may start before the attacks. Medieval Persian physicians accumulated all the existing information on medicine at that time and added to this knowledge their own observations with the introduction of many new remedies. Such information provides comprehensive data on clinical treatments based on centuries of experience in the field of headache and epilepsy, and thus might help the testing of the probable benefits of these remedies for the treatment of cephalagia and epilepsy.

Key words: Medieval Persian History, Neurological Disorders, Traditional Medicine, Ancient Physicians

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Introduction

Among the ancient civilizations, namely the Egyptians, Greek, Roman, Persian, Indian, and Chinese played important roles to form what became the nucleus and bases of medical practice. The practice and study of medicine in Persia has a long and prolific history. The Persians not only gathered existing medical information but also added to this knowledge their own astute observations and experimentation and introduced many new scientific theories. The most influential Persian physicians were Abu Bakr Muhammad Ebn Zakariya Al-Râzi (Rhazes; 865–925 A.D.)[1] Ali Ebn Al-Abbas-al-Majusi (Haly Abbas; 949–982 A.D.), Abu Ali Al-Hussain Ebn Abdullah Ebn-e-Sina (Avicena; 980–1037 A.D.), and Zinn-ol-Abedin Esmail Jorjani (Sorsanus; 1042–1137 A.D.).[2-4] The texts of Qanoon fel teb (The Canon) by Ebn-e-Sina[5], Râzi's Kitab al-hawi (The Continens)[6], Zakhireh Kharazmshahi (The treasure of Kharazmshah) by Jorjani, and Kitab-al-Maliki (Liber Regius) by Haly- Abbas[7] were central to the western medical science from the 13th to the 19th centuries.[8,9] Lectures about Ebn-e-Sina were given at the University of Brussels until 1909.[10]

The Persian academic centers like Jundishapur University (3rd century A.D.) were a breeding ground for the union among great scientists and physicians from different civilizations.[11,12] These centers successfully followed their predecessors' hypothesis and greatly extended their scientific research through history.

Due to many turbulent events in Persian territory during several centuries, numerous libraries and millions of books have been destroyed. Therefore, there is not much information about the evolution of science including medicine in ancient Persian times. The earliest Persian text that deals with health and diseases is the Avesta, a collection of Zoroastrian holy writings. It was probably compiled during the 6th Century B.C., but the precise date is not determined. The Avesta underwent various modifications and alterations; of the four texts that survive, the most popular is the Videvdat or Vendidad which was transcribed during Sasanid period. This book contains chapters about certification of physicians, medical treatment with spells, the knife and herbs. Hygienic rules and some diseases, such as epilepsy, are described in this book.[13,14]

In the Achaemenid era (529-330 B.C.), there were physicians whose knowledge was used by Greek scientists, as well as

1- Zarshenas et al., 2012: 1001-2.
2- Siraisi, 1987: 205-9.
3- Osler, 1972.
4- Elgood, 1951: 205-9.
5- Avicenna, 1988.
6- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
7- Schaltschi, 1965: 26–45.
8- Siraisi, 1987: 205-9.
9- Osler, 1972.
10- Elgood, 1951: 205-9.
11- Behrouz et al., 1993: 115-8.
12- Meyerhof, 1952: 314-5.
13- Noori, 2001.
14- Darmesteter, 1898.

those from many other nations.

Science and knowledge, including medicine, gained a significant progress during the Sassanid period (226-652 A.D.). Higher education which has an ancient past in the dynamic culture and civilization reached the peaks of prosperity at the time of the Sassanids with the establishment of centralized higher education institutions in the cities of RivArdeshir and Jundishapur from 241 A.D. onward.

Beginning with the 7th Century A.D., Persian medical practice merged with the Middle Eastern medical sciences and became an integral and indispensable part of what that usually called Islamic or Arabic medicine. Persian medicine has made a fundamental contribution to Islamic medicine. The Italian scholar, Aldo Mieli, tells us that: "The principle part of Arab science of the Orient is created by the Persians. Without any possible contestation, in fact it is to Persia that belongs the best names of these greatest of Savants such as Razi, Ebn-e-Sina and Biruni".[15]

In Persian medieval medicine, different fields were described. Among these fields, neurological disorders, especially headache and epilepsy were explained in details. Among the many studies into the history of the treatment of neurological disorders (Figure 1), the different ways in which the disorders were treated by herbal medicine are well known in Iran.[16] The aim of the present manuscript is to describe the knowledge of Persian medieval physicians on headache and epilepsy.

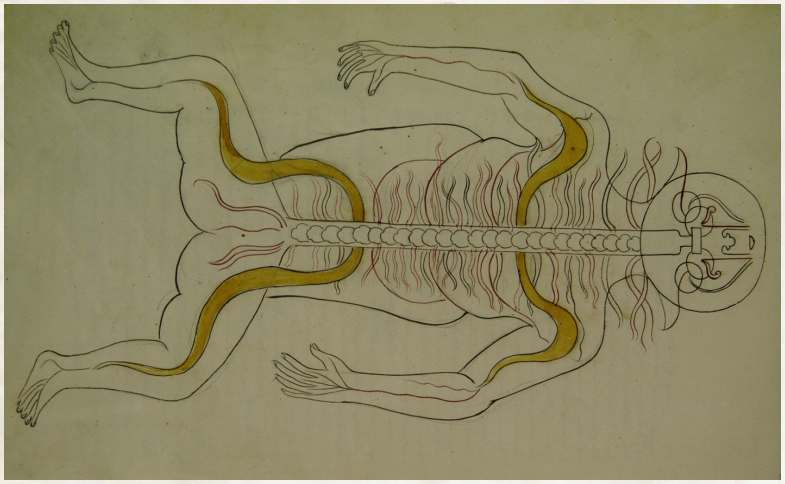

Figure 1. Anatomical pattern of the human nervous system adopted from Zakhireh Kharazmshahi by Jorjani. With the permission of the Library of Astan-e Quds Razavi, Mashhad, Iran. It is believed that this figure was designed by Mansuri.

15- Mieli, 1950.

16- Hamedi et al., 2013: 1208-18.

Headache in Medieval Persian

The medical data regarding management of headache in Persia can be traced back to the 6th century B.C.[17] However, most of the documents that outline the management of headache are derived from the medieval period. Medieval Persian physicians described the treatment of headache using many substances with different modes of actions. They attributed the therapeutic actions of plants to a specific analgesic, sedative or prophylactic drug property of variable strength.[18-20]

In the medical Persian literature, the physicians classified the headache as simple and non-recurrent (seda), recurrent bilateral (bayzeh) or recurrent unilateral (shaqhiqheh) headache. This classification system was crucial in the design of the treatment plan, which included the prescription of medicinal plants.[21,22] Bayzeh (helmet) denotes a long-duration, bilateral cephalalgia that affects the whole of the head and sometimes extends to the periorbital region. The headache is commonly excruciating in intensity, nonfluctuating, and explosive in quality. Shaqhiqheh (hemicrania) extends to the longitudinal suture that separates the left and right hemispheres of the skull. The pain in this type of cephalalgia has a throbbing quality and is associated with severe scalp tenderness in some cases; a sensation of heaviness and gastrointestinal disturbances such as nausea, hiccups and loss of appetite are other symptoms. Another type of unilateral headache described in medieval Persian medicine is highly compatible with basilar migraine as defined by the International Headache Society.[23]

Although classification of headaches in Persian medieval literatures is not matched with novel classification of headaches, some similarities such as bilateral, unilateral, sexual, fasting, pulsating, post-traumatic, catarrhal, inflammatory and alcohol-induced headache are present.[24-30]

The medieval Persian medical system put great emphasis on the inspection of the urine as a method of diagnosis. Watery urine was thought to be a sign of headache, although it might precede, accompany or follow an attack.[31,32] Amnesia, drowsiness, vertigo, fever, catarrh, paraesthesia, thirst, insomnia, high pulse rate and pulse strength, red-eye and tremor were considered symptoms of different types of headache.[33-36]

Different headache syndromes were described on the basis of aetiological factors, such as cephalalgia due to encephalitis, psychological disorders (anxiety and depression), and brain tumour.[37]

The humour theory of health and mood was a widely held

17- Gorji et al., 2002: 510-5.
18- Ibid.
19- Jorjani, 1978.
20- Zarshenas et al., 2012: 2764-5.
21- Gorji et al., 2002: 510-5.
22- Jorjani, 1978.
23- n.a, 2013: 629-808.
24- Ibid.
25- Torelli et al., 2009: 744-52.
26- Gupta et al., 2005: 715-22.
27- Solomon, 2009: 1112-5.
28- Redelman, 2010: 304.
29- Greppi, 1964: 138-42.
30- Melville, 1988: 472.
31- Rosner, 1993: 315-9.
32- Karenberg et al., 2001: 911-6.
33- Rosner, 1993: 315-9.
34- Karenberg et al., 2001: 911-6.
35- Gorji et al., 2001: 455-61.
36- Tabari, 1928.
37- Karenberg et al., 2001: 911-6.

belief in the medieval period. In this theory, all diseases result from irregular distribution of the four humours; Dam (blood), Balgham (phlegm), Safra (yellow bile), and Suda (black bile).[38,39]

Ebn-e-Sina stated that "headache results from the sudden alterations in humours or dissociation of (brain) connections". Medieval Persian physicians reported that headache could be related to environmental or biological factors. The intake of many compounds, such as wine, beer, milk, walnut (*Juglans regia*), oxymel (a mixture of honey and vinegar), cinnamon (*Cinnamomum zeylanicum*), saffron (*Crocus sativus*), mulberry (*Morus spp*), garlic (*Allium sativum*), onion (*Allium cepa*), mustard (*Brassica spp*), celery (*Apium graveolens*), myrrh (*Commiphera myrrha*), leek (*Allium porrum*), honey, cardamom (*Elettaria cardamomum*), date (*Phoenix dactylifera*), mushroom, and linseed (*Linum usitatissimum*) was thought to cause headache in susceptible individuals.[40,41]

Headache was known to be associated with some systemic diseases (such as tetanus, arthritis, and gout), neurological disorders (such as stroke and sciatica), and infectious diseases (such as visceral abscesses and scrofula).[42,43] They believed that these disorders either directly affected the brain or deteriorated the substances necessary for brain function. Medieval Persian physicians prescribed different medicinal plants for the treatment of headache (table 1). Plants have been prepared and administrated as topical, oral and nasal forms.[44]

In Medieval Persia, administration of willow oil (*Salix spp.*) was recommended for the treatment of pain in patients suffering from recurrent headaches.[45] In the first half of the 19th century, salicin, the principal active constituent of Salix spp., was isolated from the willow bark and later salicylic acid was obtained. Today, the synthetically produced conversions of salicylic acid are important analgesic, anti-inflammatory and antipyretic therapeutic compounds.[46] Acetylsalicylic acid is commonly used as an analgesic and prophylactic in different types of headaches, and reduces the frequency, duration and intensity of migraine attacks and episodic tension-type headaches. Furthermore, acetylsalicylic acid has been reported to be of some benefit during the early phases of chronic paroxysmal headache.[47] Moreover, Eugenia caryophyllata essential oil extract was shown to have an anti-inflammatory effect.[48]

38- Avicenna, 1988.
39- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
40- Avicenna, 1988.
41- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
42- Avicenna, 1988.
43- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
44- Zarshenas et al., 2013: 17-26.
45- Ibid.
46- Amann et al., 2002: 1-9.
47- Silberstein et al., 2001.
48- Öztürk, 2005: 159-63.

Table 1. Plant-derived drugs which used in medieval Persia for different type of headache treatment.[49]

Common Name	Scientific Name	Effect
	Shaqhiqheh	
Artemisia	*Artemisia absinthium* L.	Analgesic
Deadly nightshade	*Atropa belladonna* LINN.	Analgesic
Hedge bindweed	*Calystegia sepium* L.	Sedative, analgesic
Camphor	*Cinnamomum camphora* L.	Analgesic
Caraway	*Carum carvi* L.	Prophylactic
Henna	*Lawsonia inermis* L.	Analgesic
Mandragora	*Mandragora officinarum* L.	Analgesic
Myrrh	*Commiphora myrrha* (Nees) Engl.	Analgesic
Opium	*Papaver somniferum* L.	Analgesic
Pennyroyal oil	*Mentha pulegium* L.	Nerve fortifying
Spearmint	*Mentha spicata* L.	Analgesic
	Bayzeh	
Mountain fern	*Dryopteris filixmas* L.	Analgesic
Sesame	*Sesamum indicum* L.	Nerve fortifying
	Both Shaqhiqheh and Bayzeh	
Cannabis	*Cannabis sativa* L.	Analgesic
Saffron	*Crocus sativus* L.	Prophylactic, analgesic
Mustard poultice	*Brassica rapa* L.	Prophylactic, analgesic
Poppy	*Papaver somniferum* L.	Analgesic
Rose oil	*Rosa* L.	Prophylactic, nerve fortifying

Opium (*Papaver somniferum*) was a well-known compound in medieval Persia, and was used for anaesthesia during surgical procedures, postoperative pain as well as chronic pain.[50,51] Nowadays, opium and its derivatives have become the most widely used analgesics for severe and chronic pain.[52] Application of several opioids is considered effective for the treatment of intractable daily headache, episodic treatment of acute migraine or tension-type headaches, and treatment of infrequent, moderate-to-severe headaches that do not respond to standard drugs.[53]

The analgesic effect of cannabis (*Cannabis sativa*) was recognized by physicians in ancient and medieval Persia.[54,55] Cannabis was prescribed for the relief of pain in different forms of headaches. The presence of different types of cannabinoid receptors in pain processing areas of the central and peripheral nervous system and the potent analgesic effects of cannabis-like drugs indicate that cannabis and its active

49- Gorji et al., 2002: 510-5.
50- Gorji et al., 2002: 510-5.
51- Jorjani, 1978.
52- Miller et al., 2000: 299-304.
53- Silberstein et al., 2001.
54- Gorji et al., 2002: 510-5.
55- Jorjani, 1978.

constituents contribute to the control of pain.[56] The major active constituents of cannabis, tetrahydrocannabinols, have been shown to possess antinociceptive properties.[57,58] Cannabinoids produce analgesia by the activation of a brainstem circuit that is required for opioid-mediated analgesia, and control basal nociceptive thresholds through the modulation of the rostral ventromedial medulla in rats.[59] Cannabis also inhibits induction of spreading depression, a phenomena triggers migraine headach, in experimental animal models.[60]

Razi reported an apparent prophylactic effect in patients suffering from chronic recurrent headache following eating a quince (*Cydonia oblongata*) or apple (*Malus orientalis*) before breakfast. Several observations have indicated that impaired antioxidant mechanisms and an increase of reactive oxygen and nitrogen species play a causative role in different types of headaches.[61]

Persian physicians also recommended the administration of Lavendula stoechas for the treatment of trauma-induced headache. There is evidence to support the involvement of spreading depression in the induction of trauma-induced headache and migraine pain,[62] and the application of Lavendula oil has been shown to significantly inhibit the appearance of spreading depression in rat and human neocortical tissues.[63]

Rose oil (*Rosa spp.*) was believed to be beneficial in the treatment of recurrent unilateral and bilateral headaches.[64,65] Subsequent analysis revealed that rose oil contains several substances including eugenol.[66] In addition, rose oil has been shown to possess anti-conflict effects, suggesting that rose oil has anxiolytic properties.[67] Eugenol has been suggested to suppress spreading depression in in-vitro rat brain slices.[68]

In addition, the physicians in medieval Persian suggested some general recommendations to alleviate the pain of headache. The patients must avoid anything that sparked off the headache attacks (e.g., hunger, gluttony, excessive drinking and sexual intercourse, anxiety, anger, loud noise, constipation, and talkativeness). In addition, phlebotomy was recommended as an effective method for treatment of headaches. Phlebotomy from the pulsating arteries behind the ears and temporal arteries was thought effective.[69-73]

History of epilepsy in Medieval Persian medicine

Ebn-e Sina defined the epilepsy as a manifestation which begins suddenly, although premonitory symptoms, such as weakness, epigastric pressure or pain, depression, tongue

56- Calignano et al., 1998: 277-81.
57- Wilson et al., 1998: 678-82.
58- Kazemi et al., 2012: 926-36.
59- Meng et al., 1998: 381-3.
60- Kazemi et al., 2012: 926-36.
61- Gorji, 2001: 33-60.
62- Ibid.
63- Müller et al., 2006: 743-51.
64- Gorji et al., 2002: 510-5.
65- Jorjani, 1978.
66- Umezu et al., 2002: 91-102.
67- Ibid.
68- Müller et al., 2006: 743-51.
69- Avicenna, 1988.
70- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
71- Tabari, 1928.
72- Hirschberg et al., 1904: 280-90.
73- Gorji, 2003: 331-4.

paresthesia, spreading extremities paresthesia, sudden shock, incoherent speech, nightmare and sandness may start before the attacks.[74]

One kind of epileptic attack which was explained in medieval Persian textbooks is highly compatible with a complex partial seizure which becomes secondarily generalized.[75] The partial seizures were also described by Ebn-e-Sina: '... the epilepsy restricts to discrete areas such as lids, tongue or lips... and the patients are conscious during the attacks'.[76] Razi in the seventh section of his "Al-Hawi" described status epilepticus. He reported that '...and in the event that epileptic attacks are continuous and repetitive, they may lead to death. The complex relationship between migraine and epilepsy was observed by Razi. In the headache section of his 'Al-Hawi', he explained a syndrome in which bayzeh (hemicrania) and remed (conjunctivitis) precede epileptic attacks.[77]

Al-Tabari specified that the origin of epilepsy is the brain and the nerves.[78,79] The injury of the anterior ventricle results in brain contraction and elicits the epileptic attacks. It is described that the injury is provoked by some pathologic processes, such as unhealthy humor or vapour which relatively blocks the normal flow of the ventricle and the brain contracts in order to expel the harmful substances. The facial nerves follow these abnormal brain contractions.[79-81] Another mechanism of epilepsy is nerve spasms, which may originate in the brain or be induced by nerve inflammations. Ebn-e-Sina noted that inflamed nerve fibers contract in a longitudinal sense and a concomitant expansion in a latitudinal sense.[82]

The accurate observations in traditional Persian medicine emphasized the concept that many causes of seizures and epilepsy resulted from a dynamic interplay among endogenous, epileptogenic and precipitating factors. The main endogenous factors are high fever in children, pregnancy[83,84] and familial background.[85]

A variety of factors are mentioned as an extremely high likelihood of resulting in a seizure disorder. Hypoxia during delivery is a potential cause of epilepsy. The practitioners have also recognized that the infectious disease and parasitic infestation may enhance seizure susceptibility.[86]

Based on the medieval Persian medicine, therapy for a patient with a seizure disorder was multimodal and included treatment of underlying condition that causes or contributes to the seizure, avoidance of precipitating factors and prescription of antiepileptic drugs. Ebn-e-Sina described that

74- Avicenna, 1988.
75- n.a, 1981: 489-501.
76- Avicenna, 1988.
77- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
78- Temkin, 1994: 35, 85-137.
79- Avicenna, 1988.
80- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
81- Tabari, 1928.
82- Avicenna, 1988.
83- Ibid.
84- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
85- Khosravi et al., 1994:32-5.
86- Avicenna, 1988.

the choice of therapy is often determined more by specific conditions of the patient. Indeed, epilepsy classification was an important element in digesting the treatment plan in Medieval Persian medicine.[87] Ebn-e Sina and Râzi mentioned that patients must avoid swimming, cold or hot weather, staying in bath for too long, gluttony, postprandial exercise, swift motion, exhaustion, watching shiny objects, such as the sun and moon, emotional stress and excess of sexual intercourse. Migration to the temperature areas was recommended.[88]

Furthermore, diet therapy plays a crucial role in the management of epileptic patients. It is believed that the main daily meal be divided into three parts, one-third for lunch and two-thirds for dinner. Analysis of the dietetic approaches used to treat epileptics is recommended to eat food with a high potassium concentration (such as meat, cashew, nuts and fig) whereas food containing low potassium (e.g. dairy products and apple) should be avoided. In this therapeutic strategy, potassium rich food is used to treat epilepsy.[89]

Electrical-shock therapy was another way of treatment for epilepsy. Abu Al-faraj (b: 1226, Malitene, Armenia-d: 1286, Maragheh, Iran), a follower of Ebn-e-Sina, was probably the first to use electricity to treat epilepsy and neurogenic diseases by using a certain type of fish called Torpedo or cramp fish, which was put alive in water and then connected to two straps of steel. When the patient held them, which he only do for a short time, he shivered and would throw them to the ground. In his book 'Tarikh mukhtasar ad-dual' (The Abridged History of the States), he reported that after some days of this treatment the patient is cured from seizure attacks.[90] Nowadays, electric stimulation therapy is a modern treatment for several patients suffering from intractable epilepsy.

In addition, Razi recommended phlebotomy as an effective method for eliminating epilepsy when it originates from blood type humor or excess of alcohol consumption.[91,92]

Antiepileptic therapy plan in medieval Persian medicine was individualized, given different single and combined drug-therapy with a dosing schedule for each of those. The antiepileptic drugs included Lavandula stoechas[93], Artemisia dracunculus L.[94], Ferula gummosa oiss[95], beaver, mushroom mixed with almond oil, essential oil of Eugenia caryophyllata (clove oil), Pimpinella ansium[96], essential oil of Valeriana officinalis, the leaf essential oil of Laurus nobilis Linn[97], balsam oil, Foeniculum vulgare, aloe-wood, bulb (sea-onion),

87- Tabari, 1928.
88- Ibid.
89- Gorji et al., 2001: 639-40.
90- Al-Ibri I, 1992: 131.
91- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
92- Shahri, 1969: 62-4.
93- Koulivand et al., 2013.
94- Sayyah et al., 2004: 283-7.
95- Sayyah et al., 2002 (a): 105-9.
96- Karimzadeh et al., 2012: 76.
97- Sayyah et al., 2002(b): 212-6.

Anacyclus pyrethrum (pellitoey of spain), Ipomoea turpethum (turpeth), Acorus calamus and Artemisia absinthium.[98-100] Viola oil was recommended for the treatment of children epilepsy.[101]

According to Ebn-e-Sina, the prognosis in epilepsy was divided into three grades: mild (good), moderate and severe (poor). The mild degree was classified in case of seizure attacks with short duration and light postictal depression. The criteria for the severe degree epilepsy comprised dyspnea and severe anxiety before and during the attack and long-term depression after that. The moderate degree was applied to the situation between mild and severe grades.[102]

Conclusion

This article revealed some of the approaches that Persian physicians offered for the management and treatment of neurological disorders. Medieval Persian doctors accumulated all the existing information on medicine at that time and added to this knowledge by their own observations and experiments with the introduction of several new remedies. Such data provide comprehensive information on clinical management based on centuries of experience in the field of headache and epilepsy. Some of their approaches are accepted today, although most remain largely unexamined. This article represents that one should look with admiration upon the way that the Persian doctors handled their responsibility towards the patients and the findings many of which are very accurate and vivid.[103]

98- Avicenna, 1988.
99- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
100- Saneie, 1991: 133-9.
101- Abu bakr Mohamad ibn Zakariya Râzi, 1990.
102- Oritz et al., 1999: 1372-8.
103- Gorji et al., 2001: 455-61.

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