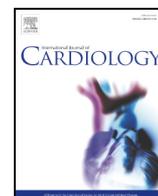




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Review

Management of stroke as described by Ibn Sina (Avicenna) in the *Canon of Medicine*Arman Zargaran^{a,b,*}, Mohammad M. Zarshenas^{b,c}, Aliasghar Karimi^a, Hassan Yarmohammadi^{a,c}, Afshin Borhani-Haghighi^{d,e}^a Student Research Committee, Department of History of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran^b Department of Traditional Pharmacy, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran^c Research Office for the History of Persian Medicine, Shiraz University of Medical Sciences, Shiraz, Iran^d Department of Neurology, Shiraz University of Medical Sciences, Shiraz, Iran^e Traditional Medicine and History of Medicine Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

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ABSTRACT

Stroke or cerebrovascular accident (CVA) is caused by a disturbance of the blood supply to the brain and an accruing loss of brain function. The first recorded observations were in 2455 BC and it has been studied intensely by ancient physicians throughout history. In the early medieval period, Ibn Sina (980–1025 AD) called stroke *sekteh* and described it extensively. Some of Ibn Sina's definitions and his etiology of stroke are based on humoral theories and cannot be compared with medical current concepts, but most of his descriptions concur with current definitions. This review examines the definition and etiology, clinical manifestations, prognosis, differential diagnosis, and interventions for stroke based on Ibn Sina's epic work, *Canon of Medicine*. The pharmacological effects of medicinal herbs suggested by Ibn Sina for stroke are examined in light of current knowledge.

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1. Introduction

Stroke or cerebrovascular accident is a disruption of the blood supply to the brain and an accruing loss of brain function. It can occur because of lack of blood flow (ischemia) caused by thrombosis or arterial embolism or by hemorrhage [1]. Stroke can cause significant physical, mental, and emotional problems in the life of patients [2].

Cerebrovascular disease is the second most common cause of death and the primary cause of disability worldwide [3]. About 80% of all stroke deaths in the world occur in developing countries [3], where the chance for a positive outcome is not favorable: people are not well-informed about prevention and the clinical manifestations of stroke [4]. Mortality rates are higher and more patients are younger adults in the labor force [5]. In addition, post-stroke care is much less well-organized [3].

Patients in developing countries are more likely to resort to traditional medicine as the sole or complementary therapeutic option [6]. Critical reappraisal of traditional sources of medical information can be a post-modern approach to finding new solutions for old problems.

Traditional Persian medicine (humoral medicine) is one of the oldest paradigms of medicine. In early medieval times (Islamic period),

Muslim physicians (mostly Persians) flourished. Their methods were based on ancient Persian, Indian, and Greco–Roman medical knowledge and from experience [7–10]. This form of medicine spread gradually throughout the world. Ancient Persian and Islamic medical treatises such as Ibn Sina's *Canon of Medicine* written in 1025 AD, Razi's (Rhazes) *Continens Liber* written circa 960 AD, and *Complete Book of the Medical Art* by al-Abbas al-Majusi (Haly Abbas) circa 970 AD were taught and used in western and eastern universities and medical centers until the 17th century [11–13].

During the Renaissance, in the transition from humoral medicine to more current paradigms of medicine, many traditional practices from ancient times fell out of favor or were forgotten [14]. A review of historical manuscripts on medical science suggests that approaches and medication developed over centuries of human experience have the potential to improve modern medical approaches and practice. Such a review, if done using a modern scientific approach and evaluation, can find novel avenues for further investigation from the writings and knowledge of pioneers in medicine. It also helps document the course of medical sciences throughout history.

This study is a review of the opinions about stroke of Ibn Sina (Avicenna), a foremost pioneer of neurology and cardiology. Ibn Sina's definition of stroke and his diagnosis and suggestions for treatment are summarized. His treatment approaches and definitions are compared with current terminology and the pharmacological effects of herbal medicines he suggested for stroke are considered. This review provides an avenue to examine knowledge and treatment of stroke in the early medieval period.

* Corresponding author at: Research Office for the History of Persian Medicine, North Ghaani Street, Shiraz, Iran. Tel.: +98 9122060881.

E-mail address: zargarana@sums.ac.ir (A. Zargaran).

2. Historical perspective

Ancient people were familiar with the manifestations of stroke. A document found in the tomb of the vizier Weshptah, an official of the 5th dynasty (2455 BC) in Egypt, describes stroke [15]. Also, it has been described in records from the Middle East by Persians and Assyrians as long as 2600 years ago [16]. The oldest scientific documented definition of stroke in a medical manuscript dates back to Hippocrates (460–370 BC) [17]. In the 4th century BC, the Alexandrian anatomists Erasistratus and Herophilus designed animal studies to simulate stroke [18]. Galen (129–200 AD) introduced four symptoms of stroke (apoplexy): respiratory pattern (deep sleep), pulse changes in response to the strength of attack, loss of consciousness, and changes in speech [19]. In China, the relationship between stroke and seizure was recognized in the 3rd century AD [20]. Paulus of Aegina classified the symptoms of stroke in new ways [21]. In the Golden Age of Islam (8th–12th century AD), Persian scholars such as Razi, al-Majusi and Ibn Sina contributed to knowledge about stroke by experimentation [8,11,22].

3. Ibn Sina

Ibn Sina (980–1032 AD) was a great influence on the progress of medicine in early medieval times [23]. He was born in *Afshaneh* in the northwest of ancient Persia. He became a physician when he was only 16 years old. He also was an expert in astronomy, philosophy, and many other branches of science. He wrote more than 400 books and treatises about these sciences, especially on medicine. His *Canon of Medicine* was in use as a medical text in Europe until the 17th century AD [11].

Current investigations show that Ibn Sina was a pioneer in cardiovascular and neurological sciences. He described the Willis circle six centuries before it was defined by Thomas Willis [14] and made pioneering discoveries in atherosclerosis [24], pulsology [25], vasovagal syncope [26], cardiovascular drugs [27], migraine [28], peripheral facial palsy [29], tremor [30], and other areas of cardiology and neurology [11,31]. Ibn Sina published two important books on cardiology: *Kitab al-Adviyat ul-Qalbiye* (Book of Medication for Cardiovascular Diseases) [32] and *Resalat-e-Ragshenasi* (Treatise on Pulsology) [33].

4. Stroke in Canon of Medicine

Ibn Sina's categorization of stroke (as the term of *sekteh*) [34,35] in *Canon of Medicine* is described herein.

4.1. Definition and etiology

Ibn Sina cited two causes of stroke. The first one is a blockage of the vessels in the brain and the second one is a blockage of the “mobile and sensitive spirit” (affective spirit) of the brain [35,36]. As seen, the first cause is very similar to current concepts, but the second can only be described using the theories of humoral medicine. Persian traditional medicine was based on four humors (*khelt* in Persian language) including phlegm or *balgham* (with cold and wet qualities), blood or *dam* (with hot and wet qualities), yellow bile or *safra* (with hot and dry qualities) and black bile or *sauda* (with cold and dry qualities). Each humor is a substance prepared from digestion and permutation of foodstuffs in GI. According to the Canon, health is due to the balance of these humors and the imbalance between them, excessive amount of each one and also abnormal humors can lead to illness [37]. On the other hand, in traditional Persian medicine, the body contains three spirits (humors): the animal spirit (*heivani*) in the heart, natural (*tabiei*) spirit in the liver, and affective (*nafsan*) spirit in the brain. Each has specific function in the body. The affective spirit transfers directives from the brain via the nervous system and could be likened to neurological pathways. The animal spirit

controls the digestive and respiratory organs via vessels that can be likened to the circulatory system [38].

Ibn Sina also divided blockage of the vessels into two categories: collapse and ischemia. He discussed blockage of the carotid arteries and the resulting stroke, which is coincident with current medical knowledge. He named the two vessels (carotid arteries) in the neck the *sobati* arteries [35,36].

According to Ibn Sina, blocking agents can be derived from blood or phlegm humors [35,36]. Fat and atherosclerosis have a phlegmatic base in traditional Persian medicine [24]. He said that the risk of hypertension and bleeding in the brain increases as blood humor increases and in persons with high blood humor nature. It can be seen that Ibn Sina connected hemorrhagic stroke (blood humor base) and atherosclerosis (phlegm humor base). Ibn Sina stated that most people with wet and cold natures are more likely to experience stroke [35,36]. In humoral medicine, fat has a wet and cold nature [38] and it can be said that people with excessive wet and cold natures tend to be overweight [39] and are prone to stroke. He also categorized stroke as severe to mild and believed that stroke usually resulted in facial paralysis.

4.2. Clinical manifestations

Ibn Sina cited the following manifestations of stroke.

4.2.1. Asphyxia

Ibn Sina believed that blocked canals and vessels of the brain can induce asphyxia. He stated that emboli or ischemia blocks the vessels [35,36].

4.2.2. Hemiplegia

Ibn Sina agrees with Socrates that hemiplegia is a symptom of stroke, but believed that sometimes bilateral paralysis can result from stroke without affecting the limbs [35,36]. He said, “the patient has no movement or respiration and seems to be dead, but is not dead.” [35,36].

4.2.3. Other manifestations

Common symptoms include headache with jugular vein engorgement, dizziness, vertigo, darkened vision, tremor, anxiety, weakness, grinding teeth during sleep, and dark urine with particles are seen [35,36].

4.3. Prognosis

Ibn Sina stated that the prognosis for patients without respiration and swallowing reflex is poor. He thought that the prognosis for patients with asphyxia and a swallowing reflex is somewhat better, but not good and that patients with difficult respiration and normal swallowing have a better prognosis. Ibn Sina agrees with Hippocrates that the treatment of the stroke is very difficult and sometimes not effective [35,36].

4.4. Differential diagnosis

Ibn Sina categorized the different causes and types of stroke in *Canon of Medicine*.

4.4.1. Cold stroke

At times, thick materials such as severe cold can lead to constriction of the brain and a type of stroke.

4.4.2. Coma

Patients who experience stroke have irregular respiration, but patients in a coma have normal respiration and will wake up.

4.4.3. Subarachnoid hemorrhage

Ibn Sina cited Hippocrates in the *Canon of Medicine* as saying that a patient who has a sudden severe headache after stroke will probably die within seven days [35,36]. This description can be attributed to dismal prognosis of subarachnoid hemorrhage. Subarachnoid hemorrhage has a mortality rate of 50% to 60% at 30 days [40].

4.4.4. Trauma

Avicenna mentioned that the symptoms of stroke may manifest after trauma [35,36].

4.5. Intervention

Medical intervention applied by Ibn Sina in the management of stroke is mainly the use of herbal medicines administered orally, nasally, topically and anally as an enema. In addition, Ibn Sina discussed the severity of stroke and recommended non-pharmacological interventions such as venesection and dry or wet cupping on the lower neck and upper back.

These procedures were most often applied to acute stroke. Ibn Sina subsequently prescribed laxative enemas with potent medicaments, suppositories of herbal exudates, and potent purgative syrups to manage the disorder. Aroma medicaments with CNS stimulant effects

were applied nasally by Ibn Sina. These medicines were administered as errhine or nasal drops [35,36].

For sub-acute or chronic strokes, Ibn Sina noted that oral and topical applications of medicaments may be beneficial. The topical application of herbal oils on the limbs was highly recommended for cerebral complications. Oral application of multi-ingredient preparations in solid or liquid forms, such as pills, decoctions, and gargles was also recommended. Massaging the feet in warm salty water and hot oils was also recommended by Ibn Sina [35,36]. Table 1 shows the different stages of stroke and corresponding treatments.

Ibn Sina recommended a number of nutritional approaches in addition to pharmacotherapy for stroke. Light and easily digestible foods containing bread and figs (*Ficus carica* L.) were recommended. Patients were recommended to refrain from drinking after a meal. Light exercise and adequate sleep were also recommended for patients affected by stroke.

Ibn Sina mentioned that fever may accompany stroke. He recommended that the physician should wait for 72 h before breaking the fever in order to ascertain its main cause [35,36].

In current pharmacology, the management of stroke is based on thrombolysis, hemodynamic stability, anti-aggregants or anti-coagulants and neuro-protection [41]. Accordingly, the present review also researched the effects of these medicaments. Table 2 shows a comparison of the results.

Table 1

Stroke phases and related treatments in Canon of Medicine.

Stroke		Type of remedy or intervention		
Phase	Dominant mechanism according to Avicenna	Step I	Step II	Step III
Acute	The stroke is caused by blood overcome	Venesection	Enema (rose water, whey and barley water)	<i>Nasal application with aroma agents having CNS stimulant activity:</i> Black hellebore flower (<i>Helleborus niger</i> L.)
Subacute	Accompanied by high phlegm concentration or excessive blood amount	Venesection	Enema (potent drugs) Suppositories (herbal exudates) Potent purgative syrups (gum euphorbium)	<i>Topical decoctions of following medicaments:</i> Dill seeds (<i>Anethum graveolens</i> L.), marjoram leaves (<i>Origanum majorana</i> L.), wormwood aerial parts (<i>Artemisia herba-alba</i> Asso), citron leaves (<i>Citrus medica</i> L.), hyssop aerial parts (<i>Hyssopus officinalis</i> L.), Shirazi thyme aerial parts (<i>Zataria multiflora</i> Boiss.), pennyroyal leaves (<i>Mentha pulegium</i> L.) <i>Topical oil application:</i> Ferula persica seeds (<i>Ferula persica</i> Willd.) and Prangos ferulacea seeds (<i>Prangos ferulacea</i> Lindl.) Olive oil with sulfur (sulfurated olive oil) <i>Topical oil application:</i> Clove fruits (<i>Syzygium aromaticum</i> (L.) Merr. & L.M. Perry), nutmeg fruits (<i>Myristica fragrans</i> Houtt.) and Elettaria fruits (<i>Elettaria cardamomum</i> (L.) Maton)
Chronic	May be accompanied by gastrointestinal upset or other internal organ damage	Emesis	Purgative agent (castor oil, pellitory oil), electuaries such as <i>Al-shailtha</i> , <i>Tiryaq</i> or <i>Baladhuri</i>	<i>Feet massaging:</i> (With warm salty water and appropriate oils) Lilly flower oil (<i>Syringa × persica</i> L.) Dill seed oil (<i>Anethum graveolens</i> L.) Marjoram leaves (<i>Origanum majorana</i> L.), chamomile flower oil (<i>Matricaria chamomilla</i> Blanco) <i>Errhine</i> <i>Gargle (multi-ingredients)</i> Shirazi thyme aerial parts (<i>Zataria multiflora</i> Boiss.) and pennyroyal leaves (<i>Mentha pulegium</i> L.) prepared in a honey oxymel. Black pepper fruits (<i>Piper nigrum</i> L.), ginger root (<i>Zingiber officinale</i> Roscoe), long pepper fruits (<i>Piper longum</i> L.) and Damask rose (<i>Rosa damascena</i> Mill.) prepared in a kind of wine or in a decoction of hyssop aerial parts (<i>Hyssopus officinalis</i> L.) and mastic gum (<i>Pistacia lentiscus</i> L.) <i>Gargle (mono-ingredient)</i> Beet root (<i>Beta vulgaris</i> L.) Loranthus fruits (<i>Loranthus europaeus</i> Jacq.) Sumac fruits (<i>Rhus coriaria</i> L.) <i>Cupping procedure</i> (Dry or wet, on lower neck and upper back)

Table 2
Medicinal plants mentioned in the Canon of Medicine for managing stroke.

Medicinal plant	Common name	Traditional name	Part used	Pharmacological effect	Study type
<i>Anethum graveolens</i> L.	Dill	Shebet	Seeds	Antioxidant [42]	In vitro
<i>Artemisia herba-alba</i> Asso	Wormwood	Afsanteen	Aerial parts	Antioxidant [43]	In vitro
<i>Beta vulgaris</i> L.	Beet	Selgh	Root	Antioxidant [44] Radical scavenging [45]	In vitro In vitro
<i>Citrus medica</i> L.	Citron	Otroj	Leaves	Neuroprotective [46]	In vitro
<i>Elettaria cardamomum</i> (L.) Maton	Elettaria	Hel	Fruits	Antioxidant [47] Blood pressure lowering, fibrinolysis enhancing [48]	In vitro Human study
<i>Ferula persica</i> Willd.	Ferula	Heltit	Seeds	Blood pressure lowering [49]	In vivo
<i>Helleborus niger</i> L.	Black hellebore	Kharbagh-e-siah	Flowers	–	–
<i>Hyssopus officinalis</i> L.	Hyssop	Zoofa	Aerial parts	Antioxidant [50]	In vitro
<i>Loranthus europaeus</i> Jacq.	<i>Loranthus</i>	Debgh	Fruits	Antioxidant, neuroprotective [51]	In vitro
<i>Matricaria chamomilla</i> Blanco	Chamomile	Baboonaj	Flowers	Neuroprotective [52] Antioxidant [53]	In vivo In vivo
<i>Mentha pulegium</i> L.	Pennyroyal	Foodanaj	Leaves	Antioxidant [54]	In vitro
<i>Myristica fragrans</i> Houtt.	Nutmeg	Jows-e-booya	Fruits	Antioxidant [55]	In vitro
<i>Origanum majorana</i> L.	Marjoram	Marzanjoosh	Leaves	Antioxidant [56] Anti-platelet [57] Neuroprotective [58]	In vitro In vivo In vivo
<i>Piper longum</i> L.	Long pepper	Darfefel	Fruits	Antioxidant [55]	In vitro
<i>Piper nigrum</i> L.	Black pepper	Felfel-esiah	Fruits	Neuroprotective [59] Antioxidant, Radical scavenging [60]	In vivo In vivo
<i>Pistacia lentiscus</i> L.	Mastic	Mastaki	Gum	Antioxidant [61] Neuroprotective [62]	In vivo In vivo
<i>Prangos ferulacea</i> Lindl.	Prangos	Jawsheer	Seeds	Antioxidant [63]	In vitro
<i>Rhus coriaria</i> L.	Sumac	Somagh	Fruits	Antioxidant, radical scavenging [64]	In vitro
<i>Rosa damascena</i> Mill.	Damask rose	Vard-e-ahmar	Flowers	Antioxidant [65] Neuroprotective [66]	In vivo In vitro
<i>Syringa × persica</i> L.	Lilly	Zanbagh	Flowers	–	–
<i>Syzygium aromaticum</i> L.	Clove	Gharanfol	Fruits	Antioxidant [67]	In vitro
<i>Zataria multiflora</i> Boiss.	Shirazi thyme	Sa'atar	Aerial parts	Antioxidant [68,69]	In vitro, in vivo
<i>Zingiber officinale</i> Roscoe	Ginger	Zanjebeel	Root	Blood pressure lowering [70] Antiplatelet [71] Antioxidant [72]	In vivo In vitro In vitro

5. Discussion

Although some of Ibn Sina's explanations for the definition and etiology of stroke are based only on humoral theories and cannot be explained using current medical concepts, most of his descriptions are very similar to modern definitions of stroke. It can be said that he explained the definition and causes of stroke in the language of his era. His discussion of the collapse of the brain and carotid arteries as causes of stroke, his close description of hemorrhagic and ischemic strokes, and the manifestations, prognosis, and differential diagnosis of stroke align with current concepts. But Ibn Sina was a philosopher as well as a physician and his major contribution to the progress of medicine was his discipline in the descriptions of each part of the *Canon of Medicine*. He categorized the subjects and compared his views with those of other physicians.

Ibn Sina's suggestions for management of stroke show that most of his suggested medicinal plants have documented pharmacological effects to control stroke. Besides the potential pharmacological advantages to managing stroke, some medicinal herbs have been proven directly in stroke by recent investigation and clinical trials. A Japanese diet that includes beet root and other vegetables was shown to reduce the rate of mortality from stroke [73]. Investigation shows that citrus fruit with inherent flavones can reduce the risk of ischemic stroke [74–76]. The effect of chamomile as a neuroprotective agent was studied in ischemic rats [52] and ginger has also been shown to reduce the risk of stroke [77]. The effect of ginger on improving oxidative stress and cognitive impairment following cerebral ischemia has also been proven [78]. Tongyan spray, a Chinese formulation in which ginger is the main ingredient, has shown a positive effect in post-stroke dysphagia patients in a randomized clinical trial [79].

Ibn Sina was one of the most prominent scientists of his era and the *Canon of Medicine* was a comprehensive encyclopedia of acquired knowledge and documentation from physicians throughout history.

Examination of the information about stroke in the *Canon of Medicine* reveals the state of human knowledge about stroke in the 10th century AD.

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