



MODE OF ACTION OF NASYA - A CRITICAL STUDY

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Abstract

Panchakarma is a method of cleansing the body of all the unwanted waste after lubricating it. Panchakarma are 5 (five) in number; hence the term PANCHA (five) – KARMA (procedures). Nasya is one among the panchakarma procedure which can perform Uttamanga shudhi. Nasa is the gate way to Shirah, the drug administered through nostrils reaches Shringataka, a Siramarma by Nasa Srota and spreads in the Murdha (Brain), taking routes of Netra (Eyes), Shrotra (Ears), Kantha (Throat) and stretches the morbid Doshas from Urdhwajatru and expels them from Uttamanga. Acharya like Charaka and Vagbhata has explained the potential mechanism of action of nasya, which when properly analyzed shows some resemblance to current theories on nasal drug delivery systems.

Key word: Panchakarma, Nasya, Mode of action

Introduction

Nasya karma is the prime treatment modality for urdhwajatrugata vikaras and one of the therapeutic procedures among pañcakarma which acts both at local and systemic levels. It is a process wherein the drug herbalized oil or liquid medicine is administered through the nostrils. Since the nose is the gateway of the head, the therapy is highly effective in curing several diseases pertaining to the head, if it is performed systematically. Though nasya has a tradition of thousands of years, intranasal drug delivery has only recently been discovered in modern science. Ayurveda has a broad umbrella for drug delivery which includes the administration of medicaments through all the navadwaras along with the inclusion of sukshmarandhra. Even though there are many routes for drug administration, uthamānga śodhana is possible only through nasya, which itself implies its importance.

Nasal route of drug administration is the natural choice for the treatment of local nasal disorders as well as other supraclavicular diseases. This trans mucosal nasal drug delivery is a non-invasive drug administration route. Due to large surface area, high vascularity, avoidance of hepatic first pass metabolism and gut wall metabolism, it has occupied a very important place in the field of drug delivery technology.¹

Anatomy and physiology of nasal tract

To understand the drug absorption of the nasal route, it is compulsory to understand the anatomy and physiology of nasal tract and how it relates to the characteristics of the delivery system used. Nasal route runs from nasal vestibule to nasopharynx which has a depth of approximately 12-15 cm. Total surface area of nasal cavity is about 180cm² and it has total volume about 16-19 ml. Mucous lines this nasal route which protects the mucosa from the inspired air.

Nasal route is divided into 3 functional zones:

1. Vestibular region
2. Respiratory region
3. Olfactory region

Vestibular region

Vestibular region is found at the opening of the nasal passage which is responsible for filtering the air coming in the nasal cavity. It is having least importance among three regions with regards to drug absorption.

Respiratory Region

It is mainly responsible for systemic drug absorption because it has highest degree of vascularity.

Olfactory Region

Olfactory region plays a very important role in transportation of drugs to the brain and CSF. Surface area of olfactory region is about 10 cm².

Mode of action –Ayurveda

In Ayurveda, the human body is compared to an upside-down tree where the head is the main part of the body and other organs are its branches. So the head controls every system, application of medicine in the form of nasya, can cure many diseases of different parts of the body. This concept is also mentioned in Bhagavad gita. Nasya is the best method to eliminate and alleviate the vitiated doṣas of urdhwanga and also it is the unique procedure for uthamāṅga suddhi.² It has different therapeutic forms of application like chūrṇa, kalka etc. acc. rogabala and rogiḅala. Nasya also ensures better absorption of the administered medicines.

According to Caraka, nose is the portal (gateway) of Siras. The drug administered through nose as nasya reaches to the brain and eliminates only the morbid doṣa responsible for producing the disease. In Astanga Samgraha it is explained that nasa being the entry to Siras (head), the drug administered through nostril reaches sringataka - a sira marma by nasa srotas and spreads in the murdha (Brain) reaches at a junctional place of netra (eye), srotra (ears), kantha (throat) siramukhas (opening of the vessels) etc and remove or detach the morbid doṣas present above supraclavicular region and expel them from the uttamanga.³

As per Caraka, the recipe administered by nasya therapy enters into the head and draws out exclusively the morbid matter since the pith (isika) is removed after removing the fibrous coating that is attached by munja (a type of grass).⁴ Susruta explained that sringataka marma is a sira marma present at the confluence of the Siras, supplying nourishment to the nose, ears, eyes, and tongues. Among the complications of nasya karma, Susruta pointed out that excessive nasal cleansing (sodhana nasya) can cause mastulunga (CSF) to flow out, depicting the significance of nasa as the gateway into Siras.

Mode of action modern view

Nasal drug administration has been used as an alternative route for the systemic availability of drugs restricted to intravenous administration. This is due to the large surface area, porous endothelial membrane, high total blood flow, the avoidance of first-pass metabolism, and ready accessibility. The nasal administration of drugs, including numerous compound, peptide and protein drugs, for systemic medication has been widely investigated in recent years. Drugs are cleared rapidly from the nasal cavity after intranasal administration, resulting in rapid systemic drug absorption.

Drug transport across the nasal epithelium is assumed to occur by one or more of the following mechanisms:

- 1) Transcellular passive diffusion
- 2) Paracellular passive diffusion, carrier-mediated absorption and secretion
- 3) Absorption through transcytosis (Figure).

Expression of efflux transporter proteins was first known to mediate multidrug resistance (MDR) in tumor cells, but may also result in reduced absorption of substrate compounds in various normal cells and epithelia. The factors influencing nasal absorption are related to nasal physiology, the physico-chemical characteristics of the compound and the properties of the specific drug formulation.⁵

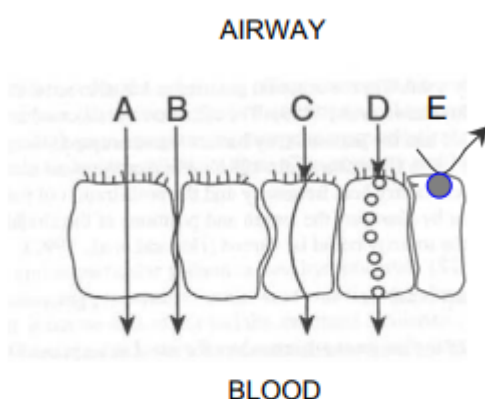


Figure 6. Potential drug transport mechanisms across the nasal epithelium: transcellular passive diffusion (A), paracellular passive diffusion (B), carrier-mediated transport (C), absorption through transcytosis (D) and efflux transport (E).

The principal step in the absorption of a drug from the nasal cavity is the passage through the mucus. Fine particles easily pass through the mucus layer; however, large particles may find some difficulties⁶. Mucus contains mucin, a protein with the potential to bind with solutes and thus affect the diffusion process. Structural changes can occur within the mucus layer as a result of environmental or physiological changes. Subsequent to a drug's passage through the mucus, there are numerous mechanisms for absorption through the mucosa. These include transcellular or simple diffusion across the membrane, paracellular transport via movement between cell and transcytosis by vesicle carriers. Several mechanisms have been proposed, but paracellular and transcellular routes dominate.

Paracellular transport is slow and passive. There is an inverse correlation between intranasal absorption and the molecular weight of water-soluble compounds. Poor bioavailability was reported for drugs with a molecular weight greater than 1000 Daltons⁶.

The second mechanism involves transport through a lipoidal route that is also known as the transcellular process and is responsible for the transport of lipophilic drugs that show a rate dependency on their lipophilicity. Drugs also cross cell membranes by an active transport route via carrier-mediated means or transport through the opening of tight junctions.

Obstacles to drug absorption are potential metabolism before reaching the systemic circulation and inadequate residence time in the nasal cavity.

The mechanism of action can be also explained in the light of different pathways

- 1) Neurological Pathway
- 2) Diffusion Method
- 3) Vascular Pathway

There is a natural protective mechanism in the nasal cavity called Nasal mucociliary clearance in which transportation of inhaled substances along with the mucus layer that covers the nasal epithelium towards the nasopharynx occurs. This process is controlled by ciliary beating with a frequency of 12 to 15 Hz) and from nasopharynx, it is swallowed. There are 3 different pathways through which substances passes from nose to brain. Substances enters into intracellular axonal transport via endocytosis/pinocytosis and then moves towards olfactory bulb which is a slow transport takes hours/days to reach the target.

Substances are translocated through the perineural space, between olfactory ensheathing cells and olfactory nerve fibroblasts, by bulk flow which is the perineural paracellular transport and is fast. The vascular pathway provides a secondary, indirect mechanism of delivery, whereby the drug is firstly absorbed into the systemic circulation and subsequently enters the brain by crossing the Blood Brain Barrier (BBB).⁷

Discussion

According to Ayurveda, nose is gateway for head. Nasya Karma is the process which eliminates the vitiated Doshas of the Urdhvanga ensuring the smooth functioning of the brain and ultimately whole body.

➤ Both Ayurveda and modern pathway of explaining mode of action of nasya has certain similarities.⁸

Pharmacokinetics	Ayurvedic comparison
Drug absorption may be through	<ul style="list-style-type: none"> • Sringhataka marma
<ul style="list-style-type: none"> • Receptor cells in olfactory mucosa 	
<ul style="list-style-type: none"> • Sensory receptors of trigeminal nerve 	
<ul style="list-style-type: none"> • Cavernous sinus 	
Circulation of drug	<ul style="list-style-type: none"> • Prana
<ul style="list-style-type: none"> • Neuronal pathway 	<ul style="list-style-type: none"> • Siramarma
(a) Olfactory (b) Trigeminal	
<ul style="list-style-type: none"> • Circulatory pathway 	
(a) Cavernous sinus	
Target	
<ul style="list-style-type: none"> • Limbic system 	<ul style="list-style-type: none"> • Psychic level of Prāna
<ul style="list-style-type: none"> • Sensory area trigeminal nerve 	<ul style="list-style-type: none"> • Sensory level of Prāna
<ul style="list-style-type: none"> • Circulation 	<ul style="list-style-type: none"> • Physical level of Prāna

➤ **Importance of supine position in nasya :**

Importance of supine position has been proven in different studies

It is important to keep the animals in a supine position in order to increase the chance for the drug to reach the olfactory region or the upper part of the nasal cavity where is direct access to the brain. In humans, the olfactory region covers about 10% of the nasal cavity with limited access.⁹

➤ **Importance of head lowered position and poorva karma**

1. Lowering of the head, elevation of lower extremities and fomentation of face - are the procedures seem to have an impact on blood circulation to the head.

2. As the efferent vasodilator nerves are spread out on the superficial surface of the face which after stimulation at surface of the face, by fomentation may the increased blood flow to the brain, i.e. momentary hyperemia.

3. It has been approximately calculated as 22% of total dilatation of cerebral capillaries caused by the facial efferent stimulation, will lead to 150% of blood inflow.

4. It is also possible that the fall of arterial pressure due to vasodilation may encounter with Cushing's reaction. In which, when the ratio between the C.S.F. pressure & cerebral arterial pressure has reduced, the increased C.S.F. pressure tends to compress the arteries in the brain causing a transient ischemia in the brain.

5. Due to this, the aroused 'ischemic response' will subsequently raise the arterial pressure (cushing). This act convinces more of 'Slush' created in intracranial space, probably forcing more transfusion of fluids into the brain tissue.

- It may possible that Nasyaaushadhithrough neurological pathway works as perception of smell is received through olfactory pathway and thus controlling various nervous and endocrinal diseases. This fact can also be supported by indication of Nasyain diseases like Pakshaghata, Avabahuka, Manyastambha, Ardita, Sangyanash, Murchha, Galganda, Aruchi, sleep disorders etc
- **Time duration after nasya karma**
- Dharana kala for nasya is mentioned as 100 matra kala

Charlton and coworkers reported that nasal drops possess higher deposition in the olfactory region compared to nasal sprays if administered to the patient in a supine position, and when formulated with mucoadhesive agents it is able to reduce the time in which the formulation is cleared from the area. The longest mean residence time in the olfactory region achieved in the study was about 14 min, compared to 1.3 min for control solution without any mucoadhesive agents

• Gozes et al. had shown with reversed phase- HPLC that (3)H-labeled NAP reaches the brain unchanged after 30 min from administration and by the 60-minute mark it reaches its maximum concentration in the brain cortex.

➤ **Why taila nasya is important ?**

Nasya drugs administered by using all possible media like aqueous media (Aavapeeda), solid particles (Pradhamana), gaseous media (Dhooma). But most preferred medium for the better action is oil media.

• The mucus is able to trap numerous molecules and deliver them to the throat where after they are swallowed into the GI tract. Therefore, drugs must pass through this mucus layer to reach the surface of the epithelium and be absorbed. Higher viscosity of the mucus causes lower clearance rate, but may also ideally allow larger percentages of doses of drugs to penetrate the mucus and reach their intended target.

➤ **Why kala is important in Nasya ?**

Goblet cells secrete mucin to create the mucus layer together with some of the nasal glands, which is turned over at varying rates (Merkus et al., 1998) depending on the environment such as humidity and temperature, but also depending on various circadian factors. Basal cells are the key cells in the nasal cavity being able to develop into all the other types, when needed

Conclusion

The Nasyaaushadhi acts on higher brain centers that control many neurological, endocrine, and circulatory functions, reaching the brain via the nasal route and having both local and systemic effects. This nasal drug administration method offers fresh promise for the administration of both local and systemic medications. For local, systemic, and central nervous system action, nasal medication delivery is a viable alternate route of drug administration. It has benefits in that it lessens systemic exposure and, consequently, side effects. Thus, the relevance of "Nasa Hi Shirasodwaram" may be demonstrated, which eventually clarifies the manner in which Nasya acts.

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