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CASE REPORT

Appropriate Timing of Medicine (*Aushadhi Sevan Kal*) Can Better Impact Patient Outcome — A Case Report of Acute Gastroenteritis (*Atisara*)

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Abstract

*Aushadh sewan kal (*ASK*)* is vital in managing the disease. ASK varies with various factors such as the disease's strength, the patient's strength, the predominance of *Dosha* (regulatory functional factors of the body), *Dushya* (which gets vitiated), etc. Precision in ASK is vital to achieve greater efficacy and a lesser quantity of medicine. Lack of this precision may produce unwanted effects. A 31-year-old female patient came to OPD of *Kayachikitsa* GAC, Nagpur, with complaints of loose motion (10 episodes), vomiting (4 episodes), nausea, abdominal pain, body aches, and general weakness since one day, headache, burning sensation in the stomach since morning. She was diagnosed with acute gastroenteritis (*Atisara*). *Atisara* treatment containing *Musta, Takra,* and *Bilvavleh* was used. After the modification of the same medicines in ASK, pain reduction and complete recovery were achieved. There was a significant decrease in subjective parameters after administering medicine in appropriate ASK. Significant improvements in *Jaran Shakti* score (Capacity to digest), *Abhyawaran shakti* score (capacity to eat), and *Ruchi* factor (appetite) were also noted. ASK is important in the administration of *Aushadha* (medicine). Negligence in ASK may decrease the efficacy of medications. This case report emphasises the relationship between *Agni* (metabolic power), gut microbiome, circadian rhythm, and ASK. This case report gives future direction for various studies to understand the interplay between *Agni* (metabolic energy), gut microbiome, circadian rhythm, ASK, and the effect of this interplay on patient outcome.

Keywords: *Atisara, Aushadh Sewan Kal,* Circadian Rhythm, Gastroenteritis, Gut Microbiome

1. Introduction

Gut microbiota contributes to the host metabolism and immunity. There are variations in gut microbiota as per circadian rhythm. These variations in gut microbiome form the vital basis for determining the precision in time of medicine administration[1]. There are alternations in the gut microbiome in Acute Gastroenteritis (AGE)[2]. AGE can be compared with *Atisara.* Symptoms of AGE are watery, loose motions, vomiting, headache, abdominal pain, nausea, and fever[3].

There is a decrease in all *Drava dhatus* in the body due to excessive water loss *(Aap dhatu)* and *Agnimandya* (diminished digestive fire) in *Atisara*. *Drava* is excreted out of the body through the anus with the help of *Apan vayu*[4]. The use of *Apan* ASK is important in *Atisar*a treatment due to the involvement of *Apan vayu*. According to *Vagbhat*, *Atisara* originates from *Amashaya* (stomach). The treatment principles are *Langhan*, *Pachan* (enhancing digestion), and *Grahi chikitsa*[5].

ASK is an essential concept in *Ayurveda,* and it explains the strength of disease, the strength of the patient, *Dosha*, *Dushya*, and *Kal* (time in the day). There are ten types of ASK (timing of medicine administration)[6]. Decisions about ASK also vary based on the predominance of the *Doshas*, *Udbhav sthan* (seat of the disease), and number of *Vega* (frequency of attack). The

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relationship between *Aushadh* and ASK is well-established in *Ayurveda* classics[7]. Though various Ayurveda practitioners are using ASK successfully according to various conditions in their practice, there needs to be more appropriate scientific evidence on PubMed about such an important concept and its probable relation with diurnal variations of the gut microbiome.

2. Patient Information

A 31-year-old female patient came to OPD of *Kayachikitsa* GAC, Nagpur, with complaints of loose motion (10 episodes), vomiting (4 episodes), nausea, abdominal pain, body aches, and general weakness since one day and headache, burning sensation in the stomach since morning. She was admitted to the Indoor Patient Department (IPD) for further management. The patient had a history of hyperacidity for two years, and she used to take antacids frequently. She was also operated on for a tubectomy five years ago.

3. Clinical Findings

The patient was diagnosed as *Sam pittatisara* based on clinical findings like yellow-coloured watery stool, vomiting four episodes, nausea, abdominal pain, body aches, general weakness, headache, and burning sensation in the stomach. She was also having burning in her anus at the time of defecation and a foul smell of stool and *Sam pita drava mala*. *Gudpaka* was not observed. Figure 1 and Table 1 summarise detailed clinical examinations.

4. Diagnostic Assessment

The patient was diagnosed with acute gastroenteritis. All routine blood investigations were done to rule out the cause. They were within normal limits except for an increase in ESR and deranged DLC, haemoglobin mentioned in Table 2. A serum electrolyte facility was unavailable in our hospital's routine pathology department. Hence, electrolyte imbalance was judged based on clinical examination and Electrocardiogram (ECG). All the baseline routine investigations are mentioned in Table 2.

Pain assessment was done using the Visual Analogue Scale (VAS)[8]. *Jaran shakti* score (capacity to digest), *Abhyawaran shakti* score (capacity to eat), and *Ruchi* factor (appetite) were accessed by the method described by Patil *et al.*,[9] summarised in Figures 2-5.

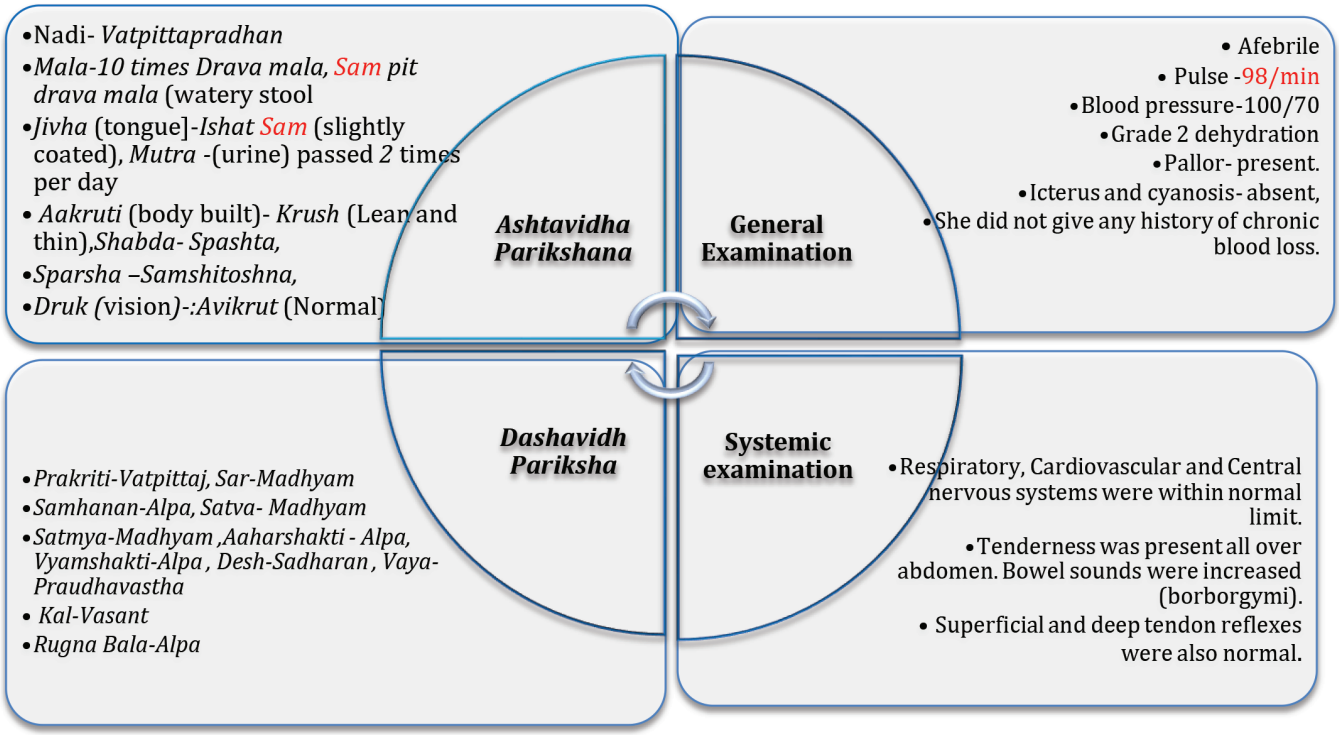

Figure 1. Details of clinical examination.

Table 1. *Strotas parikshan*

Strotas	***Stroto-dushti lakshana***
Udakvaha strotas (lymphatic system)	dryness of mouth, throat, and palate
Annawaha strotas (gastrointestinal tract)	*Anannabhilasha* (loss of appetite), *Arochak*, *Avipak* (indigestion), *Chchhardi* (vomiting)
Raswaha strotas	*Ashraddha*, *Aasyavairasya*, *Arasdnyata*, *Angamard* (body ache), *Mand Jwar* (feverish sensation), *Gaurav* (heaviness), *Aruchi* (loss of taste), *Hrullas* (nausea)
Purishvaha strotas	*Atidrava malpravritti* (episodes of loose motion)

5. Timeline (Table 3)

Table 2. Baseline routine investigations

Investigation	13/5/2019
Haemoglobin	9.9 gm/dl
TLC	6300/mm
DLCP+L+(E+M)	33%+41%+26%
Erythrocyte Sedimentation Rate	53 mm/hr
Platelet count	2.42lacs/cumm
SGOT	34.8IU/L
SGPT	29.5IU/L
Bilirubin(total)	0.22mg/dl
Bilirubin(direct)	Technically low
Blood Urea	11.3mg/dl
Serum. Creatinine	0.79mg/dl
Serum Uric Acid	3.1mg/dl
RBS	85mg/dl
BSL- Fasting	87mg/dl
BSL-Post meal	99mg/dl
Cholesterol	136mg/dl
Triglyceride	83.7mg/dl
HDL	43.9mg/dl

6. Therapeutic Intervention

Atisara is *Amashayasamudbhava* (originated from the stomach). Medicines were selected accordingly. *Awastha*-specific treatment variations are given in Table 3. Table 4 explains the Ayurveda-based rationale.

On the first day, treatment was planned to reduce *Aama* (undigested food), decrease *Dravamala Pitta*, and increase *Aap dhatu.* The patient was treated with *Pitta Shamanchikitsa* (*Pitta* palliative treatment), *Langhan* (depleting therapy), and *Pachan chikitsa* indicated in *Pittatisara*. *Laghu aahar* was given to patient considering *Alpa bala*[10]. *Narikel mashi*[11] 1gm was given in *Apan* ASK (before meal) to reduce nausea and vomiting. *Sunthi* and *Musta churna*[11] were given for local application on the forehead to reduce headaches. *Sunthi* and *Jirak*[11] are *Grahi, Deepan* (enhancing metabolic power), *Pachan*, and *Dravashoshak* (absorption of water)[12]. *Jirak* and *Dhanyak Churna*[13] were given with *Takra*[14].

On the second day, this treatment was continued except for *Musta churna*, given in *Apan* ASK orally twice a day. *Shadangodak* was given in *Muhurmuhu* ASK (continuously) to increase *Aap dhatu*[15]. *Bilva-avaleha* was given in *Vyanodan* ASK. On the third day, *Bilva-avaleha* was given in *Apan* ASK twice daily, and rest treatment continued.

7. Follow-up and Outcome

Initially, the patient was having *Alpa bal* with the above-mentioned clinical findings. After the first day, the severity of nausea, frequency of loose motions, vomiting, and headache were reduced. Abdominal pain and tenderness were present.

On the evening of the second day, there was an increase in the severity of abdominal pain, tenderness, and *Aadhman* (bloating). On the third day, all other symptoms were reduced except the persistence of abdominal pain and body aches, bloating, and tenderness compared to day 1. ASK of *Bilva-avaleha* is changed from *Vyanodan* to *Apan* on day 3. Symptoms reduced drastically after a change in ASK (Figures 3-5).

Improvement in abdominal pain was observed on day 1. It has decreased from Grade 6 to 4 just by administrating *Langhan*, *Deepan*, and *Pachan chikitsa*. On day two, it was increased from 4 to 6 by administering *Bilva-avaleha* after lunch and decreased from Grade 6 to 4 after administering *Bilva-avaleha* after dinner along with *Langhan*, *Deepan*, *and Pachan chikitsa*. On days 3 and 4, *Bilva-avaleha* was administered in *Apan* ASK along with continuing other treatments, and

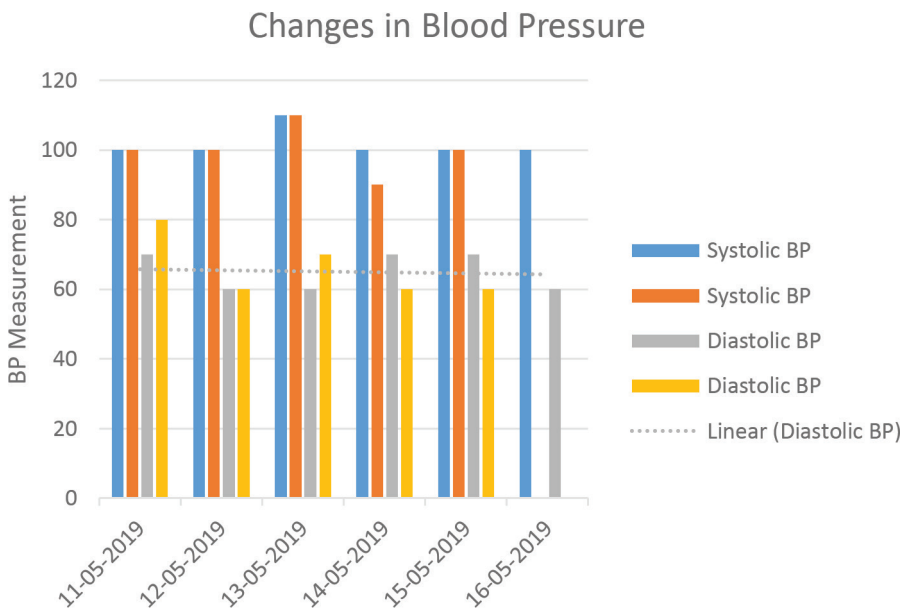

Figure 2. Shows changes in blood pressure during course of treatment.

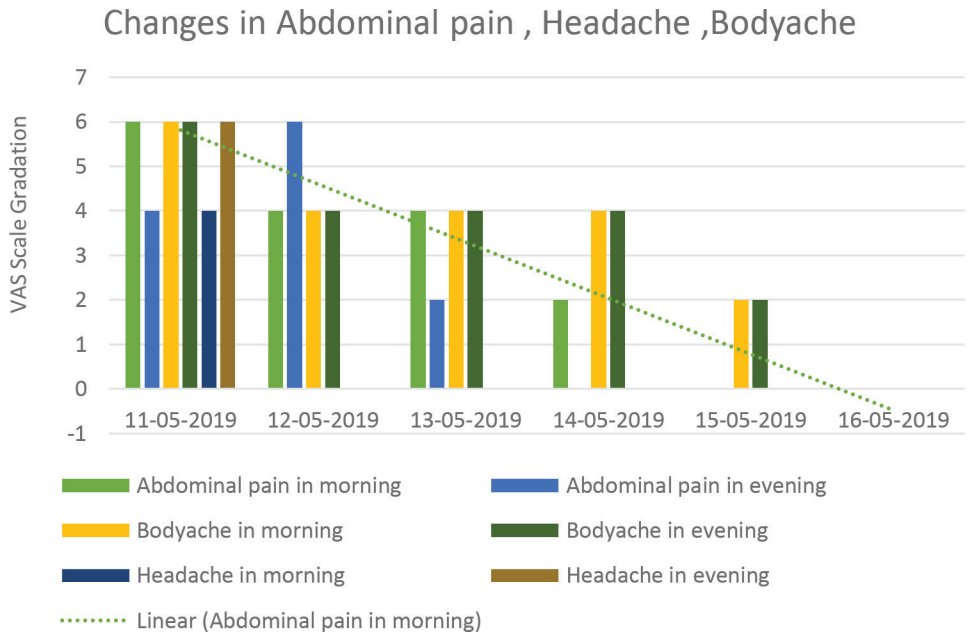

Figure 3. Shows VAS score of abdominal pain, headache, bodyache during course of treatment.

abdominal pain was reduced from Grade 4 to 2 and 2 to 0, respectively.

8. Discussion

The gut microbiome exhibits diurnal changes in its composition and function, regulated by feeding rhythm. It is well-established that there is a cross-talk between circadian rhythms and the gut microbiome[16]. The gut microbiome is also influenced by meal timing, macronutrient load, synchronization of behavioural processes, and host interactions. Various communications between the circadian system, diet, and gut microbiota highlight the importance of a time-related framework in treating multiple diseases[17]. It is also clear that multiple immune proteins have variations per the circadian clock[18]. This is also influenced by food intake and forms the scientific basis for chrono-pharmacology.

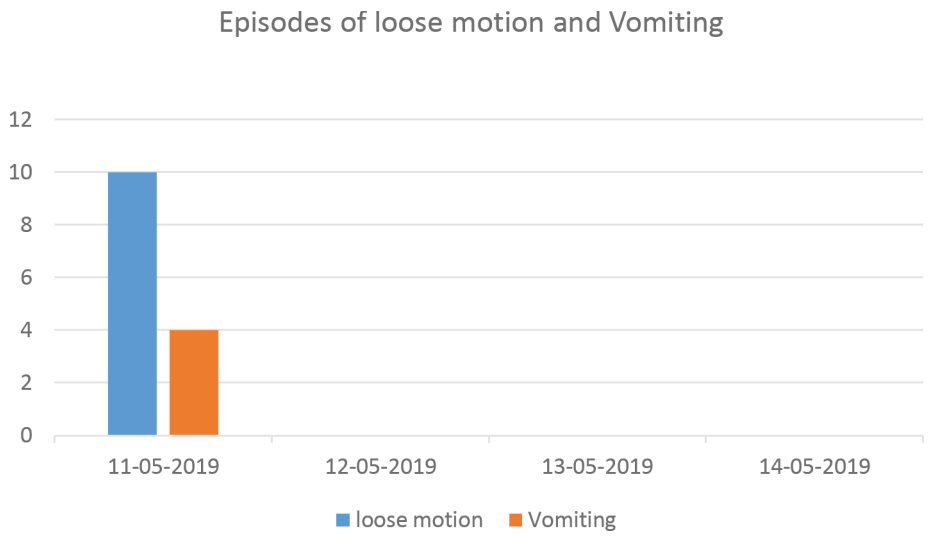

Figure 4. Shows episodes of loose motions and vomiting during treatment.

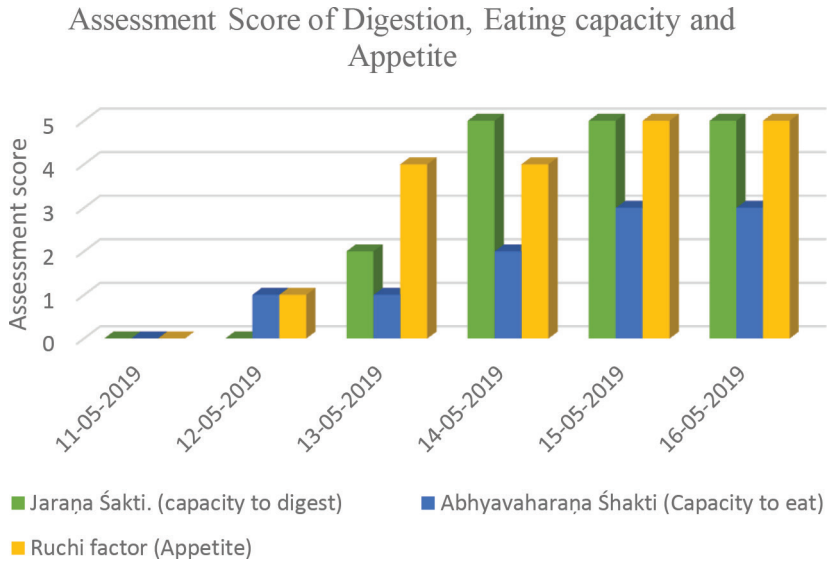

Figure 5. Shows score of digestion, eating capacity and appetite during treatment.

Ayurveda has explained these concepts while covering various aspects of *Agni*, ASK, and various *Awastha* of diseases. *Agni* is an essential component for the health of an individual. *Agni* digest and metabolize food and provide subsequent tissue nourishment. However, the change in ASK was mainly based on vitiated *Dosha* involved in the pathogenesis and site of disease. Change in ASK has also resulted in improvement in *Jathragni*. Hence, the relationship between the proper use of ASK and *Agnibala* in managing diseases needs further exploration.

Ayurveda proposes that if a drug has to act in the lower abdomen, it should be given before a meal, and if it has to act in the upper abdomen, it should be given after a meal[19]. Different ASK acts on different types of *Vayu*. For example, ASK acts on *Saman* during meals, while *Apan* ASK acts before meals. Different types of *Vayu* are related to *Agni*. In this case, the predominance of *Apan Vayu*, *Udbhav sthan* was *Aamashay*, and *Vyadhi vyakti sthan* was *Pakwashaya*. Hence, the use of different ASKs for different medicines was essential.

Apan vayu is mainly situated in *Kati, Pakwadhan* (lumbosacral region and distributed throughout the pelvic region, the visceral area below the umbilicus, genital parts), and *Sakthi* (thighs). It controls the passing of excretions, i.e., faeces and urine[20]. Medicines given

Table 3. Details of the treatment plan

Date	Treatment plan	*Aaushadhi sevan kal*	Rationale	Important event
11/5/2019	1. *Laghu aahar* (*Peya*) 2. *Narikel mashi* 1gm 3. *Takra+Dhanyak Churna+Jirak Churna* (100ml+3gm+3gm) 4. *Sunthi churna* 5gm *Musta churna* 5gm	*Apan* (before meal) *Vyanodan* (after meal) Local application at the forehead	*Deepan Pachan Grahi*	At 10 am, the patient presented with symptoms. 2 pm: Decrease nausea, no episodes of loose motion and vomiting; abdominal pain persists.
12/5/2019	CT-ALL 5. *Musta churna* 5gm 6. *Shadangodak pan* 2l 7. *Bilva-avaleha* 10gm	*Apan* (before meal) *Muhurmuhu* (continuous, i.e., frequently with or without food) *Uttarbhakta* (after meal)	*Deepan Pachan Grahi*	Increase in symptoms of Abdominal pain and tenderness. *Adhman* (~fullness of abdomen) was present in the evening; the remaining symptoms relieve
13/5/2019	CT-ALL 1 2 6 8. *Takra+Dhanyak churna+Jirak churna* 5gm 9. *Sunthi churna* 5gm *Musta churna* 5gm 10. *Bilva-avaleha* 10gm	Local application at the forehead *Apan* (before meal) *Apan* (before meal)	*Deepan Pachan Grahi*	Abdominal pain and body aches
14/5/2019	Ct-all			Body ache is present, and abdominal pain relieves
15/5/2019	Ct-all			Body ache
16/5/2019	Ct-all			Complete relief

Table 4. The properties of medicines

Drugs	*Guna*	*Ras*	*Virya*	*Vipak*	*Action*
Jirak	*Laghu, Ruksha*	*Katu*	*Ushna*	*Katu*	*Deepan, Pachan, Atisarghna, Agnivardhan*
Dhanyak	*Laghu Snigdha*	*Madhur, Katu, Tikta, Kashaya*	*Ushna*	*Madhur*	*Rochan, Deepan, Pittaghna, Strotovishodhan, Ajirnaprashaman, Shulghna, , Pipasajit, Chhaardighna*
Musta	*Laghu, Ruksha*	*Tikta, Katu, Kashaya*	*Shit*	*Katu*	*Deepan, Pachan, Pittatisarghna*
Narikel	*Guru, Snigdha*	*Madhur*	*Shit*	*Madhur*	*Pipasajit, Pittaghna*
Takra	*Laghu*	*Kashaya* *Amla*	*Ushna*	*Madhur*	*Grahi, Deepan, Pachan, Prinan, Pathya for grahani* Used in *Agnimandya, Aruchi, Atisar, Shul, Chhardi*
Bilwa	*Lahhu, Ruksha*	*Kashaya, Tikta*	*Ushna*	*Katu*	*Sangrahi, Deepan, Vaathar.*

in *Apan* ASK act on *Gudagat* vitiated *Vata dosha*[21] and digested the vitiated *Dosha* in *Amashaya* (stomach) in *Alpa Bala* patients[22]. It also strengthens the lower parts of the body[23].

In this patient, *Shadangodak* was given *Muhurmuhu* ASK (continuously) because there were episodes of loose motions and vomiting. Hence, it was possible to maintain the effect of the drug throughout the day[24].

On the second day of treatment, *Bilva-avaleha* was given in *Vyanodan* ASK. *Vyan* and *Udan* mean the administration of medicine after lunch and after dinner[25]. In this case, after giving medicine in *Vyanodan* ASK, there was an increase in symptoms of abdominal pain, tenderness, and *Adhman* (bloating). Here, the patient has been suffering from abdominal pain since admission, but the pain was relieved on the fourth day after the change in ASK, though there was an improvement in other symptoms like loose motions and vomiting.

A published case report on acute renal colic shows the relationship between gut and pain management[26]. In the Ayurveda seat of *Apan vayu* is mainly *Pakwashay* (lower abdominal part). For the action of the drug on the lower abdomen, it is given before meals, resulting in pain relief. There is a published critical review on *Bhaishajya kala* (time of drug administration) in

Ayurveda[27]. However, this case is a real example of these concepts discussed in the review. However, this is only a single case report on ASK used in GIT-related diseases, and further case reports on the use of ASK in other *Strotas*-related diseases can be future scope for studies on this topic.

9. Limitations of the Study

The objective of this case report is to provide evidence of the impact of ASK on patient outcomes.

It is difficult to prove this objective in a single case report, mainly when more than one medicine is administered to the patient as a treatment.

In modern medicine, drug intake with time, frequency, and food largely depends upon the food-drug interaction, the active half-life of the drug, its therapeutically effective plasma concentration, and its pharmacokinetics.

10. Conclusion

It is important to note that ASK of each type of *chikitsa* is important. Appropriate ASK for *Pachan* is different from ASK for *Deepan*. ASK is important in the administration of *Aushadha.* Negligence in ASK may give undesired effects or altered results than expected. ASK plays an essential role in emergency and non-emergent conditions. This case report directs various studies on the impact of ASK on patient outcomes. Clinical trials on the appropriate timing of medicine from an Ayurvedic perspective can be a difficult option; instead, analytical, observational studies can be better options.

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