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INNOVATION AND ENTREPRENEURSHIP DEVELOPMENT CENTRE

Concept of placenta with special reference to attachment of nabhinadi (umbilical cord) and its relationship with fetal birth weight

*Archana Radhakrishnan, **Anjana R., ***Sijna V.P.

Abstract

Background: Apara (Placenta) is a vital organ of higher mammals which is attached to the Garbhashaya (uterus)and is connected to the fetus through the Nabhinadi (umbilical cord). The examination of Apara (placenta) and its attachment to umbilical cord soon after its expulsion in the third stage of labour, gives a clear idea of what had happened with it in the intrauterine period of its existence. Apara, by virtue of its appearance and functions described in Ayurveda can be well correlated as placenta; and Rasavahininadi or Nabhinadi to the umbilical cord.

Objective: To evaluate the variation in placental attachment of umbilical cord and its relation to fetal birth weight. As congenital anomalies are often associated with umbilical cord insertion anomalies, early identification of the same can pick congenital anomalies

Materials and Methods: For the conceptual study, Ayurvedic classical and modern texts, books on the contemporary science, journals, presented papers and internet were reviewed. For clinical evaluation, 39 specimens were collected after proper approval from the Department of Obstetrics and Gynaecology, Alva's Health Centre, Moodbidri, for the assessment of placental attachment with umbilical cord and its diameter, thickness, perimeter, weight along with length of umbilical cord.

Discussion and Conclusion: Common attachment of umbilical cord to placenta is central. It varies at many times of attachment. Both Apara and Nabhinadi along with placenta are interrelated with each other in determining the fetal growth. There exists a positive relationship on attachment of Nabhinadi to Apara and fetal birth weight.

Key words

Apara, Nabhinadi, Placenta, Umbilical cord, Velamentous insertion of cord, Furcate

Introduction

Ayurveda describes Apara as an organ which nourishes the fetus through its attachment with the mother by Nabhinadi.[1] The normal growth and development of the fetus depend on the successful integration in functions of placenta, umbilical cord, amniotic fluid and fetal organ systems. Garbhaposhana is the main function of Apara via Nabhinadi.[2] Apara with Nabhinadi are vital organs for maintaining pregnancy and promoting normal fetal development. Examination of placenta and umbilical cord at birth can aid in identifying life threatening conditions of baby at birth.

Placenta[3] is a fleshy structure that develops mostly from fetal chorionic tissue (arising from trophoblast) and maternal decidua during pregnancy. It lies implanted on uterine wall and is connected with fetus through umbilical cord in the amniotic cavity thus maintains pregnancy and carries vital fetal functions. It also brings enormous changes in the mother, mainly through its diverse hormones, to adapt the mother to the fetal needs.

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Fetal growth is dependent on oxygen and nutrient transfer capacity of the placenta, which is highly associated with the vascular network development within the chorionic villi facilitating nutrient exchange and determining resource allocationand this organ is fundamental to fetal growth. The placental insufficiency accompanying abnormal cord insertion may increase the susceptibility to perinatal risk often associated with these conditions. Thus, it is hypothesized that optimal placentation will result in a central insertion of the umbilical cord which in turn allows an optimal growth of the fetus throughout gestation. This study aims to examine if the site of umbilical cord insertion within the placenta of singleton pregnancies could be correlated to the newborn birth weight at term and to its individual growth potential.

Materials and Methods

Study setting

The study was carried out in the Department of Obstetrics and Gynecology of Alva's Health Centre, Moodbidri.

Inclusion criteria

39 consecutive singleton deliveries after 38 weeks of gestation (WG) (from June 2013, to September, 2013), were taken for the study.

Exclusion criteria

Any history of complications during gestational period, multiple babies, any history of systemic illness or any other systemic ailments, any visible wear and tear to placenta at time of birth were excluded.

Methodology of study

During time of collection of the placentas, weight, diameter, perimeter, thickness, attachment and length of umbilical cord, weight and sex of new born, with APGAR score and gestational frequency of volunteer were recorded in the chart. The selected neonatal items were as follows: gestational age at birth (in days), baby's gender, size, and weight, and cord insertion site. Four categories were used: central insertion, peripheral insertion, marginal and membranous or velamentous. Attachment within 1cm circumference from midpoint of diameter is considered as central attachment. Attachments within 2cm from the edge of placenta is considered as marginal attachments. Attachments in between central and marginal is considered as peripheral. Attachments by membrane are velamentous and those umbilical cord which bifurcate before insertion are furcate. Each new born was individually assessed for growth and adjusted to its gestational age according to the infant's growth potential.

Instruments used

The weight of each placenta was determined by an electronic balance in kilograms and then recorded against its specific number. The indirect method used for measuring the central thickness of the placenta because of the destructive nature of direct method. A tooth pick was used to pierce the placenta from the chorionic plate to the basal plate. The central point of the placenta was determined by measuring the diameter with a plastic ruler and the midpoint thus calculated. A thick cotton thread was used to outline the perimeter of each placenta with accuracy.

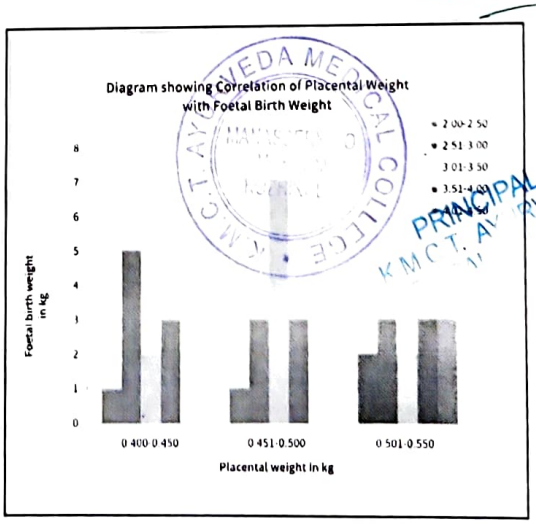
Statistical methods

Variables were described as mean and standard deviation (SD) for continuc quantitative data, number and proportion for qualitative data, and median and interquartile range for discrete quantitative data. The normality was checked with histogram of the sample data. The linear correlation between two variables by using Pearson's correlation coefficient.

Results

The mean placental weight obtained was 492.18 gm with SD of 35.740 gm. In this study, the mean placental thickness observed was 1.846 cm with SD of 0.3267 cm. The mean placental perimeter obtained in the present study was 59.13 cm with SD of 4.561cm.

Graph 1: Correlation between fetal birth weight and placental weight



In the present study Pearson's correlation coefficient obtained is, r=0.238 and p value is 0.145. There is positive correlation between fetal birth weight and placenta

Discussion

The placental weight gives us an idea about the nutritional status of the fetus. This is used to obtain the feto-placental weight ratio. Comparing the average placental weight obtained in the present study with the previous studies such as study done by Udainia et al. in 2001 (mean placental weight as 495 ± 114.11 gm with a range of 700 gm - 250 gm 104),[4] M Asghainia et al.in 2008 (mean placental weight 529.72 ± 113 gm with a range of 1200 - 250 gm 105)[5] and Peter Kwabena Appiah in 2009 (563.47 ± 132.31 gm with a range of 315to 933 gm 108.),[6] the mean placental weight reported by Udainia et al., (2001)[4] is close to the mean obtained. The Gray's anatomy textbook has given the mean placental weight as 470 gm with a range of 200-800 gm, which is close to present study[7]. The thickness of the placenta may give indirect information on the fetal-placental ratio. It may give an indication of the amount of substances (nutrients, gases) that is exchanged between the fetus and the mother. And thickness of the placenta is having a significant positive correlation with the weight of the baby. A study done by Peter Kwabena Appiah (2009)[6] observed the mean placental thickness as 2.65 cm (SD=0.55) with a range of 1.3 cm to 6.0 cm and P. O Abu et al. (2009)[8] using ultra sonography observed the mean placental thickness at 39th week as 4.51 ± 0.637cm. Another study was done by G. Reghunath et al. (2011)[9] observed the mean placental thickness as 2.1 cm. By comparing, the placental thickness obtained by G. Raghunath et al. (2011)[9] is very close to the present observation. The mean thickness observed Peter Kwabena Appiah (2009)[6] and P. O Abu et al. (2009),[8] are higher than present study. Gray's anatomy textbook has given the placental thickness as 2.5 cm and clinical anatomy by regions by Snell is given it as 2.5

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Antimicrobial Resistance (AMR): An Ayurvedic Insight

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ABSTRACT

Antimicrobial resistance (AMR) is the ability of a microbe to resist the effects of medication that once could successfully treat the microbe. Antimicrobial prophylaxis is commonly used by clinicians for the prevention of numerous infectious, but its use should be limited to specific, well-accepted indications to avoid excess cost, toxicity, and antimicrobial resistance. Rasayana drugs helps in improving immunity as well as physical strength by acting as body nourisher, improves complexion and prevents degenerative changes. Due to the improvement of immunity, microbes cannot colonize the body easily. Hence it will be protective for the body. The paper summarizes the Ayurvedic approaches which can be used effectively for prevention and treatment of bacterial diseases.

Keywords: Antimicrobial resistance, AMR, Ayurveda, antimicrobial resistance, immunity

INTRODUCTION

A microorganism or microbe is a microscopic organism, that exists in its single-celled form or in a colony of cells. The existence of unseen microbes was suspected from ancient times.[1] These single celled creatures have threatened humanity with infection which had high mortality and morbidity.[2] These microorganisms have potential to spread infection at a very rapid rate and to cause widespread epidemics.[3] In 1928, Alexander Fleming discovered the first antibiotic penicillin. By discovering this magic bullet, Fleming set the wheels in motion to create one of the most useful class of drugs in medical history.[4] Next In the next three decades there was development and discovery of a wide variety of antimicrobial agents.[5] In Fleming's Nobel Prize acceptance speech, he warned that the overuse of penicillins might, one day, lead to bacterial resistance which will be a big problem.[6]

Antimicrobial resistance (AMR) is one of the world's most serious public health problems.[7] Many of the microbes (bacteria, viruses, protozoa) that cause infectious disease no longer respond to common antimicrobial drugs (antibacterial drugs including antibiotics, antiviral and antiprotozoal drugs).[8] Antimicrobial resistance (AMR or AR) is the ability of a microbe to resist the effects of medication that once could successfully treat the microbe.[9] The term antibiotic resistance (ABR) is a subset of AMR, as it applies only to bacteria becoming resistant to antibiotics. Resistant microbes are more difficult to treat, requiring alternative medications or higher doses of antimicrobials. These approaches may be more expensive, more toxic or both. Microbes resistant to multiple antimicrobials are called multidrug resistant (MDR). Those considered extensively drug resistant (XDR) or totally drug-resistant (TDR) are sometimes called 'superbugs'.

Antimicrobial prophylaxis is commonly used by clinicians for the prevention of numerous infectious, but its use should be limited to specific, well-accepted indications to avoid excess cost, toxicity, and antimicrobial resistance. Antimicrobial prophylaxis may be considered primary (prevention of an initial infection) or secondary (prevention of the recurrence or reactivation of an infection

Action of Antibiotic

Different antibiotics have different modes of action, owing to the nature of their structure and degree of affinity to certain target sites within bacterial cells.

1. **Inhibitors of cell wall synthesis.** While the cells of humans and animals do not have cell walls, this structure is critical for the life and survival of bacterial species. A drug that targets cell walls can therefore selectively kill or inhibit bacterial organisms. Examples: penicllins, cephalosporins, bacitracin and vancomycin.
2. **Inhibitors of cell membrane function.** Cell membranes are important barriers that segregate and regulate the intra- and extracellular flow of substances. A disruption or damage to this structure could result in leakage of important solutes essential for the cell's survival. Because this structure is found in both eukaryotic and prokaryotic cells, the action of this class of antibiotic are often poorly selective and can often be toxic for systemic use in the mammalian host. Most clinical usage is therefore limited to topical applications. Examples: polymyxin B and colistin.
3. **Inhibitors of protein synthesis.** Enzymes and cellular structures are primarily made of proteins. Protein synthesis is an essential process necessary for the multiplication and survival of all bacterial cells. Several types of antibacterial agents target bacterial protein synthesis by binding to either the 30S or 50S subunits of the intracellular ribosomes. This activity then results in the disruption of the normal cellular metabolism of the bacteria, and consequently leads to the death of the organism or the inhibition of its growth and multiplication. Examples: Aminoglycosides, macrolides, lincosamides, streptogramins, chloramphenicol, tetracyclines.
4. **Inhibitors of nucleic acid synthesis.** DNA and RNA are keys to the replication of all living forms, including bacteria. Some antibiotics work by binding to components involved in the process of DNA or RNA synthesis, which causes interference of the normal cellular processes which will ultimately compromise bacterial multiplication and survival. Examples: quinolones, metronidazole, and rifampin.
5. **Inhibitors of other metabolic processes.** Other antibiotics act on selected cellular processes essential for the survival of the bacterial pathogens. For example, both sulfonamides and trimethoprim disrupt the folic acid pathway, which is a necessary step for bacteria to produce precursors important for DNA synthesis. Sulfonamides target and bind to dihydropteroate synthase, trimethoprim inhibit dihydrofolate reductase; both of these enzymes are essential for the production of folic acid, a vitamin synthesized by bacteria, but not humans.

Emergence of antibiotic resistance

India has emerged as the world's largest consumer of antibiotics with a 62% increase in popping habits over the last decade. The study "Global Trends in Antibiotic Consumption, 2000-2010," by scientists from Princeton University has found that worldwide antibiotic use has risen a staggering 36% over those 10 years, with five countries – Brazil, Russia, India,

China and South Africa (BRICS) – responsible for more than three quarters of that surge.

Antimicrobial resistance in India

Different data collected from various researches shows that bacteria attain resistance power against most of the wildly used antibiotic in India. This may cause some serious health challenges including inadequate empiric antibacterial therapy, treatment failure, problems of infection control, increased treatment expenses and increase in the spread of infectious disease caused by resistant microbes.

Factors of Antimicrobial Resistance

Environmental factors

Over the past years, the role of the environment as an important source of spread of resistance has been increasingly identified.[10] Apart from human transmission, environmental dissemination routes for resistant bacteria have also been pointed out as potential source for the spread. Environmental factors mainly including soil-related factors, animal husbandry and waste management lead to main contributing factors for AMR.[11]

Drug related factors

On the basis of various researches, human antimicrobial misuse is regarded as the greatest contributing factor toward antimicrobial resistance.[12] This is mainly due to the use of over the counter medicine without any prescription from registered medical practitioners or by irrational fix dose by practitioner. Counterfeit drugs and use of sub-standard drug acts also act as major contributing factors for induction of antimicrobial resistance.

Patient related factors

Irrational use of antibiotics may increase the resistance in individuals, on the community level and in the society as a whole. Increased trends of self-medication and poor adherence of dosage may also lead to antimicrobial resistance.[13]

Impact of antimicrobial resistance

The World Health Organization (WHO) published the first global surveillance report on antibiotic resistance (ABR) in 2014 to shown that five out of the six WHO regions had more than 50% resistance to third generation cephalosporins and fluoroquinolones in *Escherichia coli* and methicillin resistance in *Staphylococcus aureus* in hospital settings. Similarly, more than 50% resistance to third generation cephalosporins and carbapenems was reported in *Klebsiella pneumoniae*. The report attributed 45% of deaths in both Africa and South-East Asia to multi-drug resistant (MDR) bacteria. It further revealed that *K. pneumoniae* resistant to third generation cephalosporins was associated with elevated deaths in Africa (77%), the Eastern Mediterranean region (50%), South East Asia (81%) and Western Pacific region (72%).[14]

Several resistant bacteria have been increasingly involved in infectious diseases in humans, specifically, *Enterococcus* spp., *S. aureus, K. pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterobacter* spp. They are collectively termed ESKAPE and recently gained further global attention by being listed by the WHO as priority antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics.[15] All these global impact may produce major consequences related to public health in terms of longer hospital stay and increased treatment duration. It also leads to increased overall health care expenditure and reduced productive time resulting in decreased quality of life.

Concept of microbiology in classics

The microorganism and their role in producing various diseases have been elaborately described in Ayurvedic science. There are many references related to microbes in ancient literature. In Rigveda, microorganisms are described as invisible organisms having specific unique characteristics. And in Atharvaveda it is mentioned as a sukshma jantu. The classical Ayurvedic texts have documented fascinating observations about pathogenic organisms. Charaka samhitha classifies organisms into normal (sahaja) and the pathogenic or invaders (agantu). The pathogenic parasites are further classified into those that grow on the external surface or internal environment of the body termed as krimi. In various Ayurvedic classics, Acharyas have beautifully explained the term graha which capture human and produce variety of symptoms. Along with this Acharyas mentioned the spread of these microbes in terms of Janapadhodhwamsa and Aupasagika vyadhi.

Handling AMR threat through Ayurveda

Ayurveda promotes conceptual approach to *Svasthya* by stabilizing the delicate balance of nature. Ayurveda approaches act on the root cause of the disease rather than its symptoms. Through these principles, Ayurveda strategies against antimicrobial resistance can be pointed into three major objectives include-

1) Decrease the disease transmission
2) Reduce the use of antibiotic
3) Proper care after antibiotic use

For acquiring these major goals we can divide Ayurveda management into preventive, curative and convalescent care.

Prevention of antimicrobial resistance

In modern epidemiology, the concept of disease causation is explained in terms of epidemiological triad in which agent, host and environmental factors are interrelated in different complex ways to produce an infectious disease. So the prevention of any disease is mainly through the breakage of this triad. This may be achieved in three important steps:

- Source reduction
- Weakening the mode of transmission
- Strengthening the host

Prevention is the measures taken by an individual prior to the onset of any disease, which will remove the possibility of the disease occurring in the future. Ayurvedic principles related to prevention is widely accepted globally due to its safety and cost-effectiveness. Significance of modes of intervention in prevention focus on the pre-pathogenic phase. Prevention at this step is mainly categorized into primordial and primary prevention. Primordial prevention is achieved by health education. Modes of intervention in primary prevention can be focused on health promotion and specific protection. The following points mentioned can be considered for the concept of health education in primordial and primary prevention:

a. Dinacharya - Daily regimen to be followed by an individual.
b. Ritucharya - Seasonal regimen to be followed by an individual.
c. Samshodhana - Seasonal cleansing of the individual.
d. Adhaaraniya Vegas - Non- retention of the Natural urges.
e. Rasayanas - Intake of Rasayanas.
f. Sattvavijaya - Improving the mental strength with the help of Yoga and Dhyana

Health promotion concerns activities within as well as outside the health sector which include health education to increase awareness of health problems so that populations identify their health needs and become familiar with preventive strategies and the health facilities available. This is the only component which has a long-term and lasting benefit. For prevention against microbes, promote health education related to Ayurvedic basic principles like dinacharya and Acharya rasayana. Along with health education one should follow Ayurvedic specific protective measures like jala shodhana and vayushodhana.

For strengthening the host, promote health education related to daily regimen, night regimen, seasonal regimens and Acharya rasayana.[16] For the specific protection one should always consumes wholesome food, be aware about the ahara matra and kaala. Charaka emphasizes on food which are wholesome to the body like rice, green gram, rock salt, goose berry,

barley, rain water, milk, ghee, meat and honey. These should be consumed regularly for maintenance of health and prevention of diseases. One should avoid Prajnaparadha (intellectual errors), take care of sense organs, by avoiding under utilization, wrong utilization, over utilization of sense organs, and one should have good memory, knowledge about place, time and one self and should follow rules of Sadvritta to prevent diseases. The diseases due to variations in the climate can be prevented by following purification in respective seasons.[17] The rejuvenation therapy (Rasayana chikitsa) is used in the prevention and cure of disease. Rasayana like aswagandha chooma, chyavanaprasa, indukantha gritha and amalaki rasayana have its own proven immune modulatory effects against the development of infectious diseases. So by consuming all these things one should attain bala aginst disease and break the epidemiological triad.

Curative care through Ayurveda

Studies conducted in various countries have correlated antibiotic consumption with the prevalence of antibiotic resistance. Apakarsana, prakrtivighāta and nidāna-parivarjana are the basic treatment measures mentioned in Ayurveda classics against microbes. Therapeutically it can be correlated the term śodhana, śamana and nidāna-parivarjana respectively.[18] Panchakarma like Śiro-virecana, vamana, virecana and āsthāpana are pointed for apakarsana therapy.[19] Antagonist drug therapy for destruction of infectious agent and reduction of symptoms is achieved through prakrtivighāta and is performed through the drugs used in krimighna and jvarahara like Mahākashāyas.[20] Mahakashayas mentioned in our Ayurvedic classics are having Visaghna, Vranasodhana, Vranaropana and Kleda-pūyopaśosana activities. The ultimate aim of all these drug is to arrest and encounter the infection. All these antimicrobial drugs are used in the post pathogenesis phase and main action of these drug are to encounter the visha or antigen caused by the microbes symptoms produced due to the microbes like kleda, pūya, jvara, kandu, dāha etc. Krimighna, Kandughna, Kusthaghna, Jvarahara, Śvāsahara, Kāsahara, Śothahara, Śītaprasamana Mahākasāyas are to be used against these symptoms.[21] Some groups of drugs in Mahakashayas are also used to arrest the infections caused by specific type of microbes which produce different types of discharges, burning sensations, pain, redness etc. Āragvadhādi mahakashaya having Kushtagna and Kandugna activity destroy the microbes, alleviates itching and cleanses wound; Sālasārādi group is also having Kushtagna activity and administered in various types of infective skin diseases; Varunadi group is having Vranaghna activity and is highly effective in the treatment of internal abscess; Lodhrādi are yonidoshahara group which arrests the diseases of female genital tract caused by different pathogens; arkādi group help to cleanses infective wound; Surasādi group is highly effective in respiratory infection both upper and lower tract; Pippalādi group is effective in acute and chronic rhinitis; Elādi group is highly effective in boils and furuncles; Vacādi and Haridrādi both encounter the pathogens in the diseases like diarrhoeal disorders; Parusakādi is advocated in urinary disorders; Priyaggvādi and Ambasthādi both are useful in chronic type of dysentery and also effective in wound healing; Nyagrodhādi groups are beneficial for chronic wound arrests the infections in female genital tract; Mustādi group has positive result in female genital tract infections too; Lāksādi group is useful in infective wound and act as anti-helminthic; Trinapachamūla is highly effective in urinary tract infections. All the above conditions and or diseases which are arrested through the administration of different types of said groups of drugs are clinically caused due to infections.[22]

Different Ayurvedic preparations like Mahasudharshana chooma, Triphala chooma, Hareethaki chooma, Ajamodadi chooma and Dasamoola chooma are having antimicrobial activity against enteric bacterial pathogens. Studies have shown that drugs like Bilva, shalmali, Dadima, Kutaja, Arjuna and Triphala shows strong antibacterial activity against MDR *Salmonella* Typhi.

Convalescent care after antibacterial use

Antibiotics can be a very powerful factor causing imbalance of the intestinal microbiota.[23] In 1954, Bohnhoff and co-workers in their studies noticed that mice that were given streptomycin were easily infected by *Salmonella enterica* serovar Enteritidis and introduced the concept that intestinal microbiota could suppress the growth of bacteria that invade mice from the outside through colonization resistance.[24] Direct interaction of intestinal microbiota with bacteria and competition for intestinal nutrients are direct methods of inhibiting the intestinal colonization of pathogens. However, dosing with antibiotics reduces the diversity and abundance of intestinal microbiota, leading to a reduction in the competitive exclusion ability.[25] Indirectly, this destroys the community structure, thereby disturbing the interactions among microbial species and the complementary systems of nutrient metabolic pathways, resulting in widespread fluctuations in the intestinal environment. These changes are not fully reversed, even after several months of discontinuation of dosing.[26] Antibiotic-induced perturbations of the intestinal microbiota alter host susceptibility to enteric infection. Eventually, the antibiotic-induced dysbiosis of the intestinal microbiota affects the development and regulation of the immune system and increases the risk of intestine-related diseases, such as inflammatory bowel diseases and infectious diseases, in addition to diverse immunity-related disorders, such as allergic or atopic skin diseases and type 1 diabetes.[27]

These pathologies in human body may lead to Agnimandhya, Rasa kshaya, Tridosha dushti and finally end in ojakshaya. So the intervention are mainly focused to three steps

1) Repair what has been damaged
2) Re introduce beneficial bacteria
3) Rejuvenation

After attaining proper agni, next focus is to reintroduce beneficial bacteria into gut flora. For that one should incorporate probiotic in food. Kheera Ghritha Navaneetha and Takra are naturally available probiotics.

Rasayana

Rasayana helps in improving immunity as well as physical strength. It acts as body nourisher, improves complexion and prevents degenerative changes. Due to the improvement of immunity, microbes cannot colonize the body easily. Hence it will be protective for the body.

CONCLUSION

To conclude, Ayurvedic interventions can be used effectively for prevention and treatment of bacterial diseases. It can also be used in convalescent care subsequent to antibacterial therapy. Hence in the current era of AMR, Ayurvedic interventions will go a long way in reducing the risk of development of AMR and also in alleviating the adverse effects of antibacterial therapy.

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