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Urinary Odour as the Yard Stick for Suggesting Suitable Homoeopathic Prescriptions: A Review and Guide for Future Research

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Abstract

Observations of urine odour have reflective value in homoeopathic treatment, as they act as therapeutic indications for the assortment of a remedy. Urine naturally has an odour but the abnormal odour in most of the cases denotes a deviation from health. Information regarding the bacteria in the human urine is responsible for urinary tract infection (UTI), the pathogens which produces their corresponding volatile organic compounds (VOCs), that leads to abnormal urine odour is evident with recent researches. Artificial olfaction based on gas sensors and e-nose technologies also have considerable impact in identification of UTI. This article analyses the possibilities of these technological developments for finding the homoeopathic simillimum by matching the odor in samples by analyzing the volatile organic compounds with urinary odor observations on homoeopathic drug profiles. Here the clinical application of this concept depends on further studies on homoeopathic treatment of Urinary tract infection based on odor profile and thereby developing a profile of urine odour in relation to pathogens and identification of pathogen specific homoeopathic medicines. These clinical observations could be confidently used in patient care for homoeopathic medicine selection based on technology.

Keywords: E-Nose; Metabolomes; Simillimum; Urine Odour; Volatile Organic Compounds

Abbreviations: UTI: Urinary Tract Infection; VOCs: Volatile Organic Compounds; ESBL: Extended-Spectrum Beta-Lactamase.

Introduction

The possibility that urine reflect the well-being of an individual is understood since long time. Ants has been used for evaluation of urine for the presence of glucose and thereby to find diabetes by ancient Chinese physicians [1]. Charts containing details linking urine colour, taste and smell to various clinical conditions of metabolic cause were known to be used in middle ages [2].

The idea that all humans have individualistic metabolic profile that could be mirrored in their biological fluid makeup is getting interest in research [2].

Urine odour compared to other urinary parameters receives lesser attention and fewer studies in that whereas the observations on urine odour have profound value in homoeopathic prescribing. Abnormal odour of urine often indicates a medical problem which should be explored in depth. It is long felt since past till now that, the details of

human urine odour is loaded with information on physiology underlying and could throw light in comprehending the process of metabolization and excretion of compounds of lower metabolic weight. Presently the full potentialities of such volatile fraction of urine are not understood to be put into use [3].

A variety of urine odour is being observed during homoeopathic drug proving and has been used in the Homoeopathic treatment of cases with UTI. The lack is that the urine odour when utilized as curative signs are not from the perspective of volatiles with respect to microorganisms or drug proving. The observations on Homoeopathic drug proving and its clinical application in correlation with knowledge of volatile organic compounds, the pathogen, the artificial sensors provide a platform for further studies in homoeopathy for suggesting suitable medicines.

Urinary Tract Infection

Urinary tract infection is most common infections in outpatient and inpatient settings. The importance and boundaries of routine urinalysis and culture should be understood by the clinician for diagnosis of Urinary tract Infection. The assessment of urinary symptoms in relation to the diagnostic tests will help in finding the conditions such as asymptomatic bacteriuria or symptomatic urinary tract infection accurately [4].

Lower Urinary Tract Infection/ Cystitis presents as severe pain, dysuria, frequency in urination, urgency, incontinence may also have hematuria, cloudiness of urine, high smelling urine. Upper urinary tract infection symptoms include suprapubic pain, costovertebral angle tenderness, fever, chills, increased White Blood Cell count, nausea and vomiting [4].

Urinary tract Infections are mainly classified on the basis of prominent clinical features; it could be uncomplicated [5]. An uncomplicated acute urinary tract infection may be presenting with various combinations of symptoms and generally there is no underlying renal dysfunction/ obstruction [6].

Urinalysis apart from urinary tract infection can provide valuable screening and diagnostic inputs to many common diseases like malignancy, presence of protein, glucose, ketones, in urine and for renal calculi [4].

Urinalysis Interpretation

Presence of bacteria in above threshold of 1 lakh CFU/ mL in the urine is the most evident indication of urinary tract infection. Pyuria may indicate inflammation and its absence could be used to eliminate the infective cause.

Nitrates in urine is specific for bacterial infection, infection could also be present even with negative result for nitrates. Positive nitrate results show presence of nitrate reducing organisms [4].

Prevalent causative pathogens of urinary tract infections observed in study from southern part of India are extended-spectrum beta-lactamase positive Escherichia *coli*, extended-spectrum beta-lactamase negative Escherichia coli, ESBL positive *Klebsiella pneumoniae*, ESBL negative *Klebsiella. Pneumonia*, and *Pseudomonas aeruginosa* [7].

Urine analysis could be considered as the point of commencement of laboratory medicine. During earlier times physicians didn't have modern testing methods, they collected information from urine by observing its nature like colour, turbidity, smell, volume, viscosity, sweetness which are tested it modern laboratories now also. In addition to that laboratory techniques have included chemical, microscopic techniques for analysis of urine [3].

The nature that urine is a excretory product which is easily available and it is cost effective when considered form the point of laboratory analysis makes it an ideal choice for using it in preventive and therapeutic medicine [3].

Volatile Organic Compounds (VOCs)

The strong urine odour is not usually considered as an evidence for urinary infection and at the same time various methods have been used to identify the volatile markers specific to bacterial organism in urine and there by its odour. The presence of bacteria in urine and their related volatile compounds are identified in recent researches [1].

The metabolites of the pathogen or host response to pathogen or a combination of both could be the factor behind the emitting of volatiles.

Developing knowledge in this area signifies testing VOCs in urine samples. Volatile organic compound studies are increasingly being done in areas like cancer but these are limited in infectious disease studies [1].

Common bacteria and their corresponding odour are *E.coli* – Ammoniacal odour, Proteus - Burned smell, *T. vaginalis*- Fishy odour, *S. saprophyticus* - Strong smell / pungent, *Candida*- Foul smell, *Clostridium*- Fecal/putrid smell, *Strep.agalactia* - Foul smell, *Corynebacterium* - Ammoniacal odour, *Citrobacter* - Strong and pungent smell , *Strep. Fecalis*- Stinkyodour, *Kleibsella*- Smell of malt [8-15].

The idea of artificial olfaction based on gas sensors and e-nose technology may have a considerable impact in identification of UTI. To attain this sufficient knowledge of VOCs in human urine and VOCs produced by causal pathogenic bacteria's are mandatory. Several methods are used for VOC based identification of infection by pathogens. A better approach on this technology is through analysis of vapor profile of each organism, followed by designing of sensors targeting key volatiles.

Metabolome

Metabolome is small-molecule metabolites including metabolic intermediates, hormones, signalling molecules, and secondary metabolites in an organism. It is dynamic in nature and of changing nature. It is difficult to analyze the metabolomes by any individual analytical technique [2].

The area of Metabolomics finds and expresses the low molecular weight molecules called metabolites which is formed by active, living cells in various conditions and times of its life cycle.

The study of changes in the metabolic profile of a biological system during disease, toxicity or because of dietary changes is Metabolomics. Metabolomics is applied in different branches of health like pharmacology, drug trials, transplant science, screening of neonates, toxicological studies and clinical chemistry with a point that the human metabolome is yet to be characterized entirely for its fullest application [2].

Metabolomic researches work towards sequencing and measuring the numerous small molecules presenting in biological fluids during different conditions [2].

Urine Odour

The urine odour is given little clinical significance even though it is a manifest feature. Urine when passed has an aromatic odour changes to ammonia odour on standing which is due to breaking of urea. Bacterial infections produce strange strong odour. Diabetic ketones and maple syrup urine produces sweet and maple syrup odour respectively. Certain foods cause a variety of odours including pungent [3].

Causes of Urine Odour

Normally urine has aromatic odour, during bacterial decomposition or UTI ammonia odour will be present, fruit like or sweet smell when ketones are present in conditions like DM, vomiting or starving. Phyneylketonuria has a mousy urine smell, maple syrup smell odour in maple syrup urine disease. Bleachy smell in contamination, cabbage odour in malabsorption of methionine, rancid odour in tyrosinemia, sweaty feet smell in isovaleric acidaemia [3].

The notable results observed during routine urinalysis are of metabolic origin than of renal cause. Urine is a product of metabolism in body and it may have many substances which are not being regularly tested, these substances could be screened by additional laboratory techniques [3].

The requirement of such investigations could be easily found by watchful laboratory persons by its colour or odour while performing basic urinalysis. The mousy odour of phenyl-ketonuria, maple syrup urine, sweaty urine or odour of suphur in cystinuria are characteristics odours of some abnormal metabolic conditions noticed during routine urinalysis [3].

It has been reported that persons with UTIs often have urine with a pungent odor [16]. Studies also reveal that there is less relation between reporting of urine smell and likelihood of urinary tract infection [17,18].

Identification of Potential Volatile Markers and E-Nose Technology

Urine contains an intricate mixture of enormous amount of volatile organic compounds which usually alter during specific conditions and infections and could act as a possible disease marker, studies are being done in this respect concentrating on secondary metabolites. Therefore, a number of studies are being conducted by analyzing secondary metabolites produced by bacterial strains to identify urinary tract infection. A variety of urine analysis techniques and analytical methods are being used to identify volatile markers of bacterial pathogens responsible for Urinary Tract Infection.

The possibility of detecting volatile bacterial metabolites in urine for detecting urinary tract infection using procedures like GC-MS have been studied and being validated. E-noses for sensing volatiles from urine for detection of urinary tract infection and other conditions are available in the market. As a development of this strategy hitherto several volatiles produced by pathogens have been identified with a limitation of want of precision and suitability for being put into clinical use.

Sensors available commercially including e-noses based on varying technologies for identifying pathogen specific volatile profiles from urine directly and are effective in identifying urinary tract infections with convincing sensitivity and specificity. More rigorous bacterial volatile profiling with effective methodologies will be of significance for diagnosing urinary tract infection in situ [1]. The possibility of matching

such pathogen specific volatile profile with homoeopathic drug profile using sensor based volatile knowledge will be a new avenue to work on.

Homoeopathic Treatment of UTI

The anti-microbial activity of medicinal plants has been subjected to research for long time as an alternative to synthetic formulations. Medicinal active principles showed antibacterial activities against specific organisms which causes infections including typhoid, and other gastro intestinal diseases [19]. With respect to homoeopathy the anti-bacterial action of the homoeopathic medicines has been proved with various research studies [20-22].

The beneficial effect of Homoeopathy system of medicine in treating urinary tract infection is revealed in researches [23,24]. The bacterial theory of disease as perceived by homoeopathy is rather highlighted as the miasmatic theory based on which the treatment modality is followed with respect to disease and disease imitating properties of medicines. The Homoeopathy medicine information has not been studied from the view of endogenous changes in humans except the symptoms exhibited and observed as presented in Materia medica. Several attempts are being made to study the endogenous changes, one such study on "Antibacterial activity of homoeopathic drugs *in vitro*" suggests that the medicines selected on the basis of characteristic symptoms was also effective against bacteria in vitro by forming a growth inhibition area. Homoeopathy treatment acknowledges the fact that urine odour is a favoured diagnostic means which is substantiated with modern researches [25,26].

The homoeopathic view point of bacteria is based on the idea of modern bacteriology along with the strong statement that "bacteria are the results of disease, the microscopical (bacteria) are not the disease cause, but what they come after" [27]. The view point of Hahnemann, the father of Homoeopathy about contagious principle (bacteria) is explicit in his writings on chronic diseases. This and other studies have substantiated the homoeopathic view point on bacteriological techniques. This indicates that bacteriological techniques can be utilized to verify some of the basic tenets of homoeopathy [24].

The final aim of the clinical verification of homeopathic symptoms is to evaluate the strength of the link between a symptom and the efficiency of a remedy verifying at the same time the principle of similar and the totality rule. Homeopathic healing means healing according to the law of similar. All substances able to alter the state of health of a healthy subject, producing a pathogenesis of specific symptoms, when administrated to an ill living being that manifests similar symptoms to those evidenced in the healthy, work in a homeopathic way, i.e., effecting the reversibility of the morbid process. This principle of similar says that a substance, capable of provoking symptoms in a healthy organism, acts as curative agent in a diseased organism in which the same symptoms are manifested Similia Similibus Curentur, or let likes be cured by likes [28]. Clinical verification of symptoms is able to improve results in Homoeopathic practice, in this respect an evidence Based Repertory will be soon a reality [29].

Discussion

It is understood that urine odour is a definitely a connecting link between volatile organic compounds and homoeopathic drug indications the urine odour which warrants a detailed understanding. The identification of specific medicines based on the odour of urine in cases of urinary tract infection and a correlation with microorganism behind the infection and the volatiles emitted in clinical matrices representing metabolites of the infecting pathogen using human sensory or sensor based approach is not attempted in homoeopathy.

The odor in patient's urine being produced by the VOCs in urine either by the metabolites of pathogen or host responses which is observed as changes in urine odor during homoeopathic drug proving is assumed to be due to the changes in volatile organic compounds. Further characterization of urine odour with respect to urinary tract infection and other diseases is wanting. There are much studies concentrating on urinary volatile compounds as an alternative for diagnosis. Homoeopathic system has been long known for using urinary odor along with other symptoms as prescribing modality in cases of urinary tract infection and other diseases. It observes the crude smell without observing the endogenous changes, as has been done in modern days.

The feasibility of such a study is debated. However, studies on efficacy of human observation of urine odor as therapeutic indication for treatment of patients with urinary tract infection is justified here.

As Materia medica in homoeopathy are not from the point of view of VOCs, the studies based on human sensory observations of urinary odour in patients with urinary tract infection when compared to Materia medica may clear a pathway to analyze the homoeopathic prescription using urinary odour as indication on the basis of metabolites of the infecting pathogens or pathogen induced host responses or a combination. Further studies linking the urine odour, VOCs, their corresponding pathogens, and the homoeopathic drugs throw light into the concept that urinary odor could be used as yard stick for choosing suitable homoeopathic

prescription.

Conclusion

Researches could be conducted for substantiation of homoeopathic indications of urinary odour for treatment of Urinary tract infection and application of such knowledge in other diseases too since homoeopathic treatment indications could be generalized. Observation of pathogen specific odour from homoeopathic point of view necessitates exploring the feasibility of drug proving targeting volatile organic compounds, thereby applying human sensory approach or artificial olfaction based on gas sensors, e-nose sensor technology for homoeopathic medicine selection.

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