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Using concentrations of calcium and oxalates to predict crystalluria type

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ABSTRACT: The majority of the analyzed calculi from patients are composed of calcium oxalate (CaOx) monohydrate whewellite (Wh) and CaOx dihydrate wedellite (Wd). The urinary calculi were identified by chemical and morphological analysis based on106 urine samples from human voluntary. The Crystalluria made by an optical polarized light microscopy. The oxaluria and urinary calcium were determined by conventional volumetric assays. The aim of this paper was to develop a simple system to predict and classify the type of crystalluria using Artificial Neural Networks (ANNs) algorithm.

KEYWORDS: calcium oxalate; urinary calculi; Artificial Neural Networks.

1 INTRODUCTION

The Lithogenesis includes all the processes driving the development of stone in the urinary tract. Lithogenesis includes several phases which are expressed successively simultaneously[1]. The main and major factor resulting in crystal formation is supersaturation as the primary event in lithogenesis that is a process during which, the oversaturation of urines by the lithogenic substances behind the formation of crystals. These crystals can in certain conditions and according to the oversaturation degree, agglomerate may lead to the formation of urinary stones in the urinary system generating renal failure in human. In fact the urine composition (inlithogenic substances) has an important role and driving force in stone development. In fact the prevailing tendency of urolithiasis is increasing across the world [2, 3]. It is caused by several factors that include frequently CaOx crystalluria in the urine. It crystallizes in the form of (Wd) and (Wh) [2, 4- 8]. The previous studies have been indicated the variations in Ox concentration induce greater and important effects on CaOx supersaturation and in the number and size of CaOx crystals.Also have been indicated that the risk of forming CaOx crystals depends on both Ca and Ox concentrations, namely on the CaOx molar product, whereas the crystalline phase of CaOx, either mono or di-hydrate, depends on the molar ratio of Ca to Ox [9]. During diagnosis of the disease, no precise decision can be easily made taking into account the individual concentrations of calcium and oxalates those individually. While it is necessary to introduce the two important variables CaOx molar product (pCaOx) and the molar ratio calcium / oxalate (Ca/Ox) in order to ensure a better diagnosis [10]. It appears from the results of most studies in the literature that CaOx is the most frequent and majority urinary crystals crystallize [11- 16]. Previous studies have shown that the combined consideration of Ca and Ox molar products and ratios may afford a better prediction of both the probability of forming CaOx crystals and the type of CaOx crystals than does the separate consideration of urinary Ca and Ox concentrations [9]. However, rarely are the studies dedicated to the investigation of the influence of the calciuria and the oxaluria on the formation of the crystals CaOx in urines. As a matter of fact, the crystals are a promoting phase to the formation of urinary stones. The work of Daudon et al. in 1987 on the study of oxalo-calcium crystalluria nephrolithiasis of subjects have shown the influence of the product of the concentrations molar urinary calciums and oxalates (pCa.Ox) and their ratio (Ca / Ox) on the crystallization of CaOx. Daudon et al. in 2004 confirm that the motor of the crystallization of CaOx is the molar oxalocalcique product, but the crystalline form in which it is observed in the urine is highly dependent on the ratio molar calcium / oxalate [18]. It has been shown that the main determinant of the crystallization was the molar product oxalocalcique (pCaOx) Daudon et al. in 1989, also that crystal form whewellite or weddellite depends mainly (but not exclusively) of molar (calcium / oxalate (rCa / Ox) Daudon et al. in 2015. The observations, values Crystalluria and oxaluria are confirmed by those of Daudon et al in 1987. The results obtained in our laboratory [21] showed that there is

a strong correlation between CaOx crystalluria and the urinary concentrations of calcium and oxalate. calciuries and oxaluries values even approximate, may allow to predict the formation of oxalate crystals calcium. The influence of the calcium concentrations and oxalate (Ca. and Ox) was valued. The presence of cristalluries increases with the concentrations of calcium and oxalate, on the one hand and with their products (pCa.Ox.) and ratio (Ca / Ox.), on the other hand. In the present work, the ANN algorithm has been applied, in order to classify the subjects of the database into 3 classes, depending on the chemical concentrations of variables (Ca, Ox, pCa.Ox, and Ca / Ox) and on their clinical status. The first class contains subjects presenting a Wh crystal type. The second class contains subjects with a Wd crystal type and the third one includes subjects who are unaffected by this disease. According to the obtained results of the classification, we developed a simple intelligent diagnosis system. This system is important for medical laboratories since it can provide useful information about the development, formation of the urinary stones. The determination of the crystal types of the urinary stones would be helpful to better manage, economically and socially, the treatment of this rising disease [16].

2 MATERIALS AND METHODS

2.1 DATASETS

MORPHOLOGICAL ANALYSIS

The first phase of the analysis is the determination of the morphological type of crystals according to the classification (Daudon M. et al., 1999). The morphological analysis was conducted in accordance with the published protocol. The study was carried out on 106 urine samples from human volunteers from the region of Tadla Azilal.; all samples were analyzed and prepared in our laboratory [21]. Crystalluria has been characterized using optical polarized light microscopy.

CHEMICAL ANALYSIS

The apparent oxaluria and urinary calcium were determined by conventional volumetric assays on urines. The database contains 63 men and 43 women among whom 30 (28.3%) cases presented (Wh) crystal type their urine, 27 (25.5%) cases presented a (wd) crystal type and 49 (46.2%) cases would be not affected by this disease (Nc). Table 1 shows the distribution of study subjects according to age group and gender.

Table 1. The 106 samples according to age group

Group	<20 years	20-40 years	>40 years	Total
Man	5	34	24	63
Woman	5	21	17	43
Global	10	54	42	106

2.2 DATA ANALYSIS

ALGORITHM OF ARTIFICIAL NEURAL NETWORKS

The Artificial Neural Networks (ANNs) are used in various disciplines such as economics, ecology, environment, biology and medicine. These networks are applied in particular to solve problems of classification, prediction [22-24], categorization, optimization, recognition of the forms and the associative memory [25]. The ANN improves the diagnosis in medical sciences. The ANN was applied in order to determine the chemical composition of urinary stones and to classify them [26]. In fact, the ANNs are used, for example, in cases of the prediction of myocardial [27, 28], lung pathologies [29, 30], diabetes [31], cancers [32], Alzheimer's disease [33] electromyography and kinesiology [34]. In an ANN, the Neurons are connected via synapses (connection links), that modulate signals passing through them. Each synapse has an associated weight w. The net input N is the function of all transmitted signals Xi and their corresponding weights Wi in a neuron: $\mathrm{N} = \sum \mathrm{Wi}\ \mathrm{Xi}$ (sum of weighted input signals). Each neuron applies an activation (transfer) function to its net input N in order to provide an output signal for each neuron. A neural network is characterized by its architecture or its pattern of connections between the neurons (see fig1). Several research works were made to describe the functioning of ANNs [35-37].

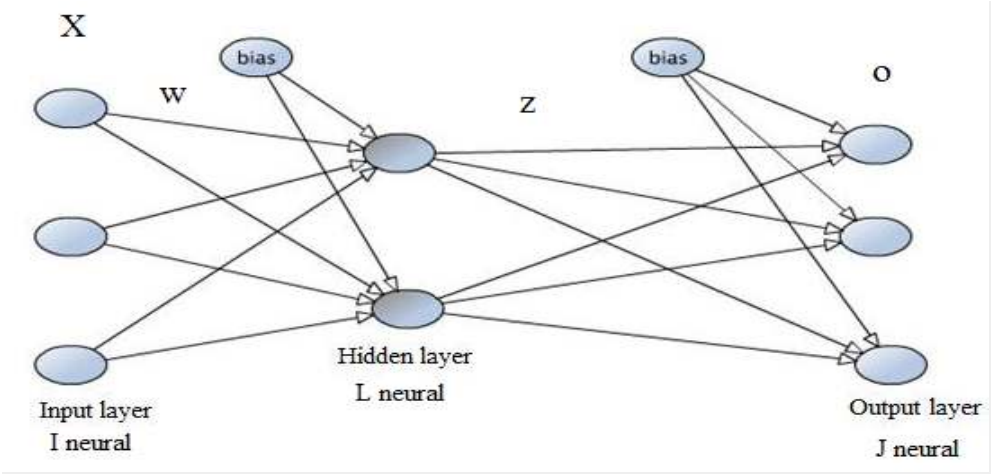

Fig. 1. Neural network architecture Je propose de supprimer ce qui suit car trop deconnécté du reste et peu explicite pour ceux qui ne conniassent pas les ANN.

3 RESULTS AND DISCUSSION

The determination of calciuria and oxaluria, even approximate, can allow predicting the CaOx crystal formation in the lithogenic patients urines. The differentiation of crystalline phases of cristalluries is important in the search for causes crystal growth or even lithogenesis. Otherwise, if information is disclosed too late it will be difficult to assess the usefulness and relevance of the information. The study of the spontaneous crystalluria is source essential information for the etiological diagnosis and medical management of patients with urinary stones or crystal pathologies likely have deleterious consequences for the function renal. It should be practiced in all laboratories to enable better detection of risk factors and more effective monitoring of patients suffering from urolithiasis [18]. In this study two main objectives of this work: the first objective was the search of the offending parameters in the development of urolithiasis. It should be noted, in agreement with previous work that the calculi remain the irreplaceable source of information on his training and analysis by appropriate physical techniques leading to the knowledge of its chemical composition allows access to the etiology of urolithiasis. Also, crystal growth is the decisive step of lithogenesis in which the crystallizable certain substances in urine. Therefore, the study of crystalluria is crucial in understanding the mechanisms that govern the initial phase of development of urolithiasis. The second objective was to study the influence of CaOx concentrations on the formation of urinary crystals as well as to classify and identify urinary crystalluria type based on these parameters using Algorithm of Artificial Neural Networks. The complexity of the neural network is measured by the number of neurons in the hidden layer. The number of hidden layers and the number of neurons from layer have an influence on the quality of learning. The choice of number of hidden layers is empirical.

After the results, The error prediction rate, using ANN, is 0.165 for Whewellite, 0.066 for Weddellite and 0.083 for Nc. (see table II). It should denote that in Spite of Our technique for studying the influence of urinary calcium and oxaluria on the crystallization whewellite and weddellite proved preliminary and limited in terms of the approximate chemical assay techniques the best average correct prediction achieved was 89.53% using ANN algorithm.

Table 2. the Correct classification and Errors rate of AAN algorithm

	Wd	Wh	Nc
Correct classification rate	83.50%	93.40%	91.70%
Errors Rate	16,50%	6,60%	8,30%

The Chemometrics coupled to simpler and less expensive chemical and physical analyses (volumetry and optical microscopy), on the one hand and methods of data analysis, on the other hand would be a quick and less expensive tool for a first diagnosis of the urolithiasis that can allow the decision-makers to avoid the high budgets, of coverage, assigned to the treatments of this disease.

Thanks to ANN algorithm, we have been able to establish a decision-making model allowing the competent sanitary services to predict the lithogenous risk in the populations. The study of crystalluria is an excellent review of laboratory that brings many benefits to the diagnosis and management of kidney diseases crystalline origin [40]. The results of most works in the literature showed that CaOxs is the most frequent as chemical species in urine and the majority of stones are crystalluria [10- 15]. However, rarely are the studies dedicated to the investigation of the influence of urinary calcium and apparent oxaluria on the formation of CaOx crystals in the urine; that is the initial step on the formation of urinary stones. These crystals can in some conditions become stones that lead to the failure of the urinary system.

4 CONCLUSION

Having a new tool to get more information out of the determinations of urine calcium and urine oxalate can be helpful for the clinic especially as it is in the form of a computer algorithm that does not need to cost much time and money. Our system predicts that the person will form specific crystals this may in theory be used as a marker for stone growth. This has not been proven yet but would be of clinical interest since stone growth may be the process that turns a harmless plaque or plug into a harmful stone. And predict that someone will form the crystalluria type this will be of help for the removal procedure. This work has shown that ANN algorithm is very powerful method to develop a simple diagnostic system since it achieved a good predictive performance and yields the highest average correct prediction rate.

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