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Review – Stone Disease

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Metabolic Work-up of Patients with Urolithiasis: Indications and Diagnostic Algorithm

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Abstract

Context: The incidence of urinary tract stone disease is increasing and the risk of recurrent stone formation is high. Appropriate therapeutic procedures with the aim of counteracting the progress of stone formation are highly desirable. Metabolic work-up is considered essential as a base for optimal design and follow-up of effective recurrence prevention.

Objective: To scrutinize the current literature with regard to principles of metabolic work-up for this heterogeneous group of patients.

Evidence acquisition: Relevant articles in PubMed, guideline documents, consensus reports, and the Cochrane Library published during the past 20 yr were consulted.

Evidence synthesis: Grades of recommendation were used according to the principles applied in the European Association of Urology and American Urological Association guidelines. Medical efforts to prevent recurrent stone formation should be part of the care of patients with urinary tract stone disease (grade of recommendation A). A careful medical history and imaging together with analysis of stone composition, blood, and urine provide the basis for appropriate measures, but the treatment has to be individualized (grade of recommendation D). Whenever possible, stone analysis should be carried out at least once for every patient or each time when a long time has elapsed between two stone episodes because the risk factors explaining stone formation may have changed (clinical principle). The medical history, including information on dietary and drinking habits as well as lifestyle, is necessary for appropriate advice (grade of recommendation C). The medical history, together with imaging and stone composition, is used to estimate the severity of the disease (clinical principle). Identification of specific medical conditions should be supported by blood and/or urine analysis (grade of recommendation B). Pharmacological agents associated with an increased risk of stone formation should be identified (grade of recommendation C). Patients who have formed noncalcium stones should always be given recurrence preventive treatment. Analysis of urine composition for these patients is optional, but might be of value in the follow-up to support decisions on appropriate dosage regimens (grade of recommendation C). For patients with idiopathic calcium stone disease information from 24-h urine samples should be used, although the number of samples to be taken is debated (grade of recommendation C). Information from 24-h urine analysis should be used for selective dietary and drinking advice as well as for selection of the most appropriate pharmacological agent (grade of recommendation B). The treatment effects on the risk of stone formation can be followed by estimates of supersaturation based on urine composition (grade of recommendation C).

Conclusions: It is clear that the metabolic work-up of patients with urinary tract stone disease should be individualized according to stone type and severity of the disease, and that the different therapeutic approaches are closely associated with the availability of therapeutic tools and motivation by the patient.

Patient summary: Effective prevention of recurrent stone formation is determined by several factors such as the current and previous stone episodes and surgical procedures, stone composition, medical history, dietary and drinking habits, lifestyle, and ongoing pharmacological therapy. Analysis of blood and urine is an important part of the metabolic evaluation, but how extensive the risk evaluation should be is determined by the type of stone and the severity of the disease.

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1. Introduction

There is an increasing incidence of urinary tract stone disease worldwide [1], and the recurrence risk is high. The purpose of metabolic evaluation of patients with urolithiasis is to identify possible risk factors considered responsible for or contributing to this pathology. It thereby is assumed that therapeutic correction of any observed abnormality or deviation might counteract future stone formation and favorably affect the course of the disease.

There are several sources from which information on risk factors can be obtained in order to provide a basis for the most suitable and optimal treatment of patients with urolithiasis. It might thus be necessary to include, in the workup, stone composition, imaging, medical history with information on dietary as well as drinking habits, and lifestyle. Moreover, it is useful in patients with a high level of suspicion for a genetic cause of recurrent stone disease to get information on possible genetic risk factors. Further input in the diagnostic procedure is obtained from analytical results of blood and urine. It needs to be emphasized, however, that the details of stone formation in many parts are incompletely understood.

In this brief review, the intention has been to summarize which information can be obtained from the different sources listed above. The evidence or consensus presented in the literature was used to provide a recommendation for the best clinical management of patients with urinary tract stone disease.

Apart from procedures directly required for surgical considerations, it is fundamental for all further decisions on metabolic evaluation and treatment-in its widest sense-that there are some medical recurrence preventive tools that can be offered to the patient [2-8]. Almost every patient is very interested to know why he/she formed the stone(s). Unfortunately, this interest is not always reflected in long-term adherence to given medical advice or treatment. Before starting an extensive metabolic work-up, it therefore is also important to find out how motivated the patient might be for further analytical and therapeutic procedures [9]. Taking into consideration that the main focus of the present review is to evaluate methods for measuring the potential risk of further stone formation and that the recurrence preventive measures essentially are outside the scope of this report, it is not possible to discuss how the metabolic work-up should be designed without also at least indirectly touching on the possible treatment alternatives.

A number of treatment options have been described and used clinically, most of them with the aim to decrease the risk of forming critically supersaturated urine with regard to the precipitated salt, to increase inhibition of crystal nucleation, growth, and aggregation, or to favorably affect all these factors. Almost all clinical decisions in this regard are based on findings in final urine, that is, urine with a composition similar to that in the bladder, renal pelvis, or calyces. Most reports on urinary risk factors discussed in the literature refer to analysis of the composition of 24-h urine, and the diurnal variation is seldom accounted for. Insufficiently convincing arguments and a generally reluctant attitude to metabolic work-up and biochemical care among a majority of urologists have resulted in increased surgical rather than medical treatment of this large and heterogeneous group of patients. It is our hope that the content of this review will disclose what we can get from a careful metabolic work-up.

2. Evidence acquisition

The data on which the recommendations in this article are based were acquired from several current guideline documents, recently published consensus documents, Cochrane reviews, as well as several relevant articles published during the last 10 yr and accessible in PubMed. Furthermore, the information comprises logical conclusions based on our current understanding on how urine composition is thought to affect the final steps in stone formation. In the latter regard, it was also necessary to consider a number of reports on recurrence prevention. Although it is always desirable to carry out a literature search and review according to Preferred Reporting Items for Systematic Review and Meta-analyses standards, this was not the particular remit of this manuscript and was also difficult with this particular subject due to the paucity of high-quality evidence.

3. Evidence synthesis

3.1. Current stone situation and medical history

A reasonably informative medical history and appropriate imaging are almost always parts of the initial examination of every patient who presents with urinary tract stone problems. How extensive the further work-up should be is determined by several factors and needs to be individualized [10]. For that purpose, the previous history of stone formation, the current stone situation, and what kind of stone(s) the patient has formed are important decisive factors.

The medical history should have the aim of identifying specific diseases and abnormalities, which are known to be associated with stone formation and commonly reflected in altered composition of urine. Some of the most common medical conditions are summarized in Table 1. It is, moreover, of importance to search for possible genetic factors that can explain stone formation [11].

It has been emphasized in the American Urological Association (AUA) guideline document [9,10] as well as by Robertson [3] that the medical history should contain questions with the aim of getting information on both nutritional and lifestyle aspects. Of particular interest is knowledge of the average daily intake of fluid, calcium, sodium, and protein, as well as consumption of fibers, vegetables, and food stuffs rich in oxalate. Consumption of fructose (soft drinks) is also of importance. This information is fundamental to individual dietary and lifestyle recommendations [3,10,12]. It has been observed that excessive consumption of animal protein might affect urine composition by increasing calcium and oxalate and by

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