From "Max-Planck-Institut für Kulturpflanzenzüchtung"
Hamburg
(Director: Professor Dr.R.v.Sengbusch)

Technical and Clinical Aspects of the Dissolution of Renal Calculi in the Human Body.

by M.Brozinski, G.Kallistratos, W.Knothe, I.and W.Noddack, R.v.Sengbusch, I.Sücker, A.Timmermann.

(Lecture held by Dr.A.Timmermann at the Sixth Meeting of the Nordrhein-Westfälische Gesellschaft für Urologie on April 22, 1961 at Bad Oeynhausen)

First informations concerning application of the compound EDTA (ethyl diamine tetra acetic acid) as a solvent for renal calculi in the human body were published in June 1960.

The basic principle of renal calculus dissolution is the transformation of its water-insoluble chelate complex. A solution of 2,5% of the bi-sodium salt of the a.m. acid buffered by 3% tri-ethanol amine on a pH of 8.6 effects entire dissolution of all formations of calculi containing calcium oxalate. Particles of uric acid compounds in mixed concrements also become soluble by transformation into tri-ethanol ammonium urate.

Physiological toleration of the solution of this salt was tested in thousands of rinsing hours in both the animal and human body. We have already reported on chemolytical, clinical treatment (literature).

According to Sarre's statistics on chemical formation of human renal calculi 95% of them can be dissolved by this solvent (literature).

Meanwhile new and more effective solvents on the basis of Lithium compounds of EDTA have been proposed by Professors I.and W.Noddack. These solvents with their laboratory descriptions P.2o and P.3o are at present under clinical test. Being especially well tolerated they render better results.

(P.2o = 3% Lithium salt of EDTA, molar prop.abt. 3:1
plus 0.5% tri-ethanol amine, pH 8.5
P.3o = 5% Lithium salt of EDTA, plus 1% tri-ethanol amine, pH 8.5)

After their composition our treatment has been entirely changed to the application of the solvents P.2o and P.3o.

Lately Sücker has tested a group of compounds effecting an especially good dissolution of phosphate concrements of calculi. It is a sodium solvent of the EDTA with the molar prop. sodium:EDTA = 3:1, corresponding to a tri-sodium salt. A compound of 5 % of the salt buffered with 1 % of tri-ethanol amine is in the scope of pH above 8 being favorable for the formation of Ca-complexes. This compound with its laboratory description P.4o is well tolerated and has an extended possibility of application on oxalate and phosphate concrements. *)

*) later added information

.../2

The dissolution of the renal calculus in the human kidney is carried through with the aid of a double-channel catheter effecting continuous rinsing of the calculus' surface. Two sizes of catheters are being used: 9 and 12 Charrière.

Generally the 9 Charrière catheter will be sufficient for treatment. Severe infection of the kidney and numerous calculi, however, may necessitate an increase of rinsing capacity which, after tissues have become adapted to rinsing, may be gained by exchanging the 12 Charrière catheter through the stretched urethra. Catheters are being well tolerated by the ureter and may remain there for weeks.

Insertion of the 9 Charrière catheter is to be carried out with the aid of the normal size cystoscope, the 12 Charrière with adequate calibre, requiring only anaesthesia of the urethra's mucous membrane (Pantocain o,2%) after the patient had received a general sedative (Dolantine, Cliradon etc.) by injection.

The insertion of the rinsing catheter necessitates an extreme lordosis in order to attain maximum wideness of the urethra. As the rinsing catheter which is made of plastics at a temperature of 37° C. is rather rigid and inflexible it will, therefore, have to be heated in a water bath up to 8o-9o° C. prior to insertion. For some minutes it will lose its rigidity and will follow the curves of the urethra. Insertion thus becomes easy to handle and practically no discomfort will be caused to the patient. After some minutes the catheter will regain its former rigidity eliminating alteration of position despite the peristalsis of the urethra.

After insertion of the rinsing catheter's jet into the calciform system its location will have to be checked upon by X-ray examination. Attention will have to be paid to the fact that all lateral openings of the jet are located within the cavity of the renal pelvis.

The most eminent prerequisite of continuous rinsing of the renal pelvis is the unhampered return flow of the solvent. This demand is met by the especially wide calibre of the catheter's out channel, by the free position of the rinsing jet inside the renal pelvis and by a new-developed suction vacuum in the container receiving the out flowing solvent. Suction capacity for a continuous flow of the solvent will have to be kept at a pressure of o.1-o.2 atü. The removal of tiny blood clots and flakes of mucus may demand a temporary increase up to o.5 atü. Such an increase of suction efficacy does not imply any danger to the kidney. A vacuum of o.1-o.2 atü effects a more intensive flow of 5oo-6oo cm^3 per hour as compared to a mere 15o cm^3 without the aid of a vacuum. In addition pressure can also be brought to bear through the infusion burette and will thus add to the increase of flow. Here also o.1-o.2 atü will be sufficient.

Both measures combined provide for a flow of 2.ooo cm^3 per hour.

.../3

An increased speed of flow virtually implies an abbreviation of calculus dissolution as the factor of kidney urine thinning down the solvent is almost eliminated and alteration of pH value is kept at a minimum.

The closer the contact between the lowest jet opening and the calculus' surface is the more effective the solvent will be. Therefore X-ray checking on the jet's location within the renal pelvis during insertion becomes essential. Provided attention has been paid to all prerequisites rinsing itself will prove to be painless. Patients are made familiar with all facts and technical detail of the treatment and they soon will be able to take an active part regulating their own rinsing by adjusting pressure in case of minor disturbances. Although this will favourably distract them and will be of actual help frequent checking up by the nursing personnel cannot be dispensed with.

In case the catheter gets clogged rinsing will have to be discontinued for at least some hours. In many cases small blood clots, flakes of mucus or fragments of calculus will spontaneously be excreted. If, however, the catheter remains obstructed it will have to be exchanged; removal of it is simple and painless. 24 hours should then elapse before re-insertion takes place.

Normally a 8-1o hours' rinsing can be carried through with patients treated in hospital.

Body temperature of the patients during treatment is generally normal, in some cases sub-febrile. Fever, however, indicates acute pyelitic condition due to disturbances of liquid circulation in the renal pelvis. In this case rinsing is to be entirely discontinued for some days.

Now increased intravenous medication of antibiotica is indicated and the effect is to be augmented by a slow rinsing with physiological NaCl-solution to which a concentration of antibiotica of 1/oo has been added.

Nearly always the blood descent reaction is slightly increased. There will be values between 2o-4o mm during the first hour and 4o-6o mm during the second. Numbers of leucocytes in the blood may rise whereas haemoglobin- and ery-values may fall in the course of a longer treatment. These effects vary greatly and still ask for firm explanations as to their causes. Minor blood transfusions are then to be performed in order to balance losses and to improve general well-being. Treatment of year-long kidney infections in combination with a calculus filling all renal cavities or renal fistula with calculi ask for frequent checking on blood values and general condition.

Examination of the calcium level of the blood prior to and after the daily rinsing does not show any great deviations from normal standards. Values vacillate between 8,9 and 1o,1 mg %.

..../4

Up to now in all cases of chemolytical treatment antibiotica were employed as a precautionary measure as to check bacteria activity. Daily or every second day patients receive intravenous injections of 250 mg of a general antibioticum. It will have to be ascertained whether such quantities are indispensable or not. Occasionally observed anaemia may possibly have been caused by this measure. But so far no harm to the digestive system has been noticed. During treatment patients receive vitamine compounds.

Bacteriological examination of urine prior to rinsing treatment shows mixed infections originating from different bacteria. Also during treatment bacteria are present. Examinations of patients who had undergone rinsing treatment 1.1/2 years ago showed that their urine was sterile. After conclusion of clinical treatment patients receive diet perscriptions and medicaments in order to prevent harmful acidity of the urine.

With male patients special attention will have to be paid to the prostata. Frequently an inflamed implication of the male annexes coincides with an infection of the ureter. The increased sensitivity of these organs then makes insertion more complicated and in addition causes dysury during treatment. Daily massage of the prostata, hot sitting baths and occasional injections of Depot Cyren (15 mg or more) render relief.

With female patients a longer rinsing catheter of 130 cm ought to be employed so that the joinings of in- and out tubes can easily be connected - distant enough from the thighs.

Chemolysis without any complication will soon become oppressively tedious to the patient and reading, radio, television along with a varying diet will gain special bearing. Also light massage of extremities will be of advantage as the repose of the long rinsing hours causes growing uneasiness.

With regard to treatments hitherto carried through we can now safely say that the dissolution of one ore more calculi in the renal pelvis which lie open to the solvent is technically simple. Calculi in the calciform system can also be treated successfully if the opening of the renal pelvis is wide enough. Duration of rinsing is, however, still difficult to predict.

The question whether continuous rinsing implies damage to the function of the renal parenchyma cannot be definitely answered as yet. Intravenous pyelograms made immediately or some days after conclusion of treatment showed prompt, symmetrical secretion of the contrast substance. On the treated side the contours of the renal calix appeared coarsened, typical for pyelitides. Control examination some months later showed normal function. Pathological nitrogen-value remnants could not be made out in the blood serum.

.../5

With a 3o year old patient whose single kidney had been operated upon one year ago 2 bean-sized recidivous calculi were dissolved by P.2o in 9o hours. Remnants of nitrogen values stayed normal during treatment also in this case. Blood descent reaction and leucocyte values showed a slight, temporary increase. Examination of concentration capacity resulted a top concentration of 1.o2o. Inasmuch continuous rinsing is to be blamed for the decrease of function cannot be argued in the case of this anamnesis.

The question of the formation of recidivous calculi in already treated kidneys can only be considered with with restraint as time for observation and statistical material are inadequate. But up to now there have not occured any recidivous formations where total dissolutions or partial dissolutions leaving small fragments had taken place. On the contrary, smaller fragments tend to decay and in due course are being spontaneously excreted. In only two cases treatment had to be interrupted - due to the patients' lack of time - leaving rather large calculi in the calix. After one year both showed considerable growth.

Of the 3o patients who hitherto had undergone chemolytical treatment radiographs will be demonstrated.

(Demonstration)

Conclusion

We have endeavoured to compile a survey on clinical application of results gained in laboratory research aiming at intra-renal dissolution of renal calculi in the human body.

We are of opinion that on the basis of facts already attained further development of this method will be answerable.

Future only will be able to allot the proper place to chemolytical treatment of renal calculi as compared to surgical therapy.

Latest tests proved solvents P.2o and P.3o to be best.
Their compositions are as follows:

P. 8 = 2.5% Di-sodium salt of EDTA + 3% tri-ethanol amine
P.2o = 3 % tri-lithium " " " + o.5% " "
P.3o = 5 % " " " " + 1% " "
P.4o = 5 % tri-sodium " " " + 1% " " *)

*) later added information