VASOPRESSIN EFFECT DURING THE DIURETIC AND THE RECOVERY PHASE OF ACUTE RENAL FAILURE

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The well known polyuria of patients recovering from acute renal failure has been ascribed either to overhydration during the oliguric phase, or to osmotic diuresis (Bull, 1956). However, one has also to consider a decreased response to antidiuretic hormone (ADH), as suggested by De Wardener (1961).

In the present investigation the ADH response has been studied in normal individuals and in patients in the diuretic stage and after recovery from acute renal failure.

![Graph showing response to vasopressin injection:]

*Fig. 1. Normal response to oral hydration (2% of body weight, followed by continued administration of water in hourly amounts equal to diuresis). Normal response to intra muscular injection of 5 IU of vasopressin.*
**Methods**

Urine was collected and blood samples were taken every hour during 9 hours after oral hydration with water to an amount of 2% of body weight. During the experiment water administration was continued in hourly amounts equal to diuresis. In each sample osmolality, sodium and creatinine were determined. Osmolality determinations were made by cryoscopy on a Fiske osmometer type G62, sodium was measured by emission flame photometry on an Eppendorf flame photometer.

Creatinine was determined by the method of De Vries and Daatselaar (1955).

**Investigations**

In normal individuals creatinine U/P ratio, that is Urine creatinine concentration in mg %, markedly falls when water diuresis occurs, as one would expect.

After intramuscular injection of 5 I.U. of vasopressin, antidiuresis occurs with a sharp rise of urine osmolality from below 100 to approximately 700 mOsm/kg with an equal rise of urine electrolyte concentration and creatinine U/P ratio.

Plasma osmolality and total electrolyte excretion per hour remain constant (Figure 1).

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**Fig. 2.** Male (60 yrs), recovering from acute renal failure (12th day of diuretic phase). No increase of diuresis after oral hydration. No significant change of urine osmolality after vasopressin injection.
In Figure 2 the data are presented of a 60-year-old man recovering from acute renal failure after cholecystectomy complicated by post-operative shock. The oliguric phase lasted three weeks. On the 33rd day of renal injury, creatinine clearance was 23 ml/min and BUN 33 mg%. Virtually no diuresis and change of urine osmolality occurred after ingestion of the standard amount of water nor after injection of 5 I.U. vasopressin. Creatinine U/P ratio and urine electrolyte concentration remained constant.

Identical results were obtained in a 30-year-old male, suffering from genuine epilepsy during the early polyuric phase of acute renal failure as a result of a severe status epilepticus. His data are presented in Figure 3.

At the time of the experiment creatinine clearance was 23 ml/min. and BUN was 75 mg%. Neither hydration nor vasopressin injection were effective and the results were similar to those in case 1.

The experiment was repeated in the same patient 19 days later on the 33rd day after onset of diuresis. BUN at this time decreased to 13 mg% and creatinine clearance increased to 100 ml/min.

A marked but definitely subnormal and delayed decrease of urine osmolality occurred after water loading and a minute effect of vasopressin was noted as shown in Figure 4.

Vasopressin effect was less pronounced, definitely delayed and transient in comparison with the normal response. It may be of interest that gradual decrease of urine osmolality after forced drinking of water was only temporarily inhibited by injection of vasopressin.

In Figure 5 results are presented of forced water drinking and vasopressin injection in a woman of 33, one month after the onset of acute renal failure, caused by miss-matched blood transfusion during a pelvic operation.

Fig. 3. Male (30 yrs), acute renal failure (14th day of diuresis). No increase of diuresis after hydration. Minimal increase of urine osmolality after 5 IU of vasopressin intra-muscular.
Fig. 4. Same patient as in Figure 3. The experiment was repeated on the 33rd day of diuresis. Decrease of urine osmolality after oral hydration is delayed and subnormal. Delayed, shortened and diminished effect of vasopressin injection.

Fig. 5. Female (33 yrs), acute renal failure, 14th day after onset of diuresis. Definite but subnormal responses to water loading and vasopressin injection. Creatinine U/P ratio increased nearly in the normal way.
The experiment was done on the 14th day of diuresis, creatinine clearance was 72 ml/min. and BUN was 11 mg%. Responses to water loading and vasopressin injection were both decreased but more closely resembled the normal pattern than in the previous cases. Creatinine U/P ratio increased to nearly normal.

The experiment was repeated in the same patient 5 months later and is presented in Figure 6.

Oral hydration resulted in normal diuresis and decrease of urine osmolality. Creatinine U/P ratio showed a normal response, a pronounced anti-diuretic effect of vasopressin was observed and urine osmolality sharply rose to 600 mOsm/kg. This rise was however definitely shortened and was limited to only one hour.

A third experiment was done in the same patient 9 months after the renal injury. The results, presented in Figure 7 showed the same pattern as five months before, namely normal diuresis, normal decrease of urine osmolality and creatinine U/P ratio after oral hydration. A pronounced but still diminished and shortened antidiuretic effect was observed after vasopressin injection.

![Graph showing the results of the experiments](image-url)

**Fig. 6.** Same patient, 5 months after recovery from acute renal failure. Normal increase of diuresis and normal decrease of urine osmolality after oral hydration. Normal response of creatinine U/P ratio after vasopressin injection with sharp, normal rise of urine osmolality. Vasopressin effect however is definitely shortened and limited to 1 hour.
Fig. 7. Same patient, 9 months after acute renal failure. Vasopressin effect is still subnormal and shortened.

Conclusion

It may be concluded from these experiments that

1. Response to oral water loading and vasopressin injection in high doses is absent in the early diuretic phase of acute renal failure.

2. During the recovery phase responses to both stimuli return slowly.

3. After recovery is apparently complete and creatinine clearance has returned to normal, the effect of a vasopressin injection is still shortened.

4. The abnormal renal response to vasopressin during recovery from acute renal failure may be of clinical importance.

REFERENCES


DISCUSSION

The Chairman: Any questions, please?

Dr. E. J. Dorhout Mees (Utrecht): The influence of vasopressin can be judged only when you know the osmotic load that is presented to the tubules. I have not seen on your graphs these parameters, and I think it is not possible to distinguish between the two courses you mentioned in the first minutes—whether this concentration effect is due to osmotic diuresis or to tubular defect though probably the last thing is true. But in the earlier days certainly there is an osmotic diuresis; where you have an osmotic diuresis it is impossible to get a concentrated urine and a high creatinine-urine/plasma creatinine ratio.

The question I should like to ask is what were the creatinine and urea levels during these experiments?

Dr. R. Grijm (Amsterdam): You are right—in the diuretic phase you cannot expect a vasopressin effect, but in the follow-up of these patients, when the creatinine clearance has been returned to normal (more than 100 ml/min) there is no reason for an osmotic effect. The most important thing I wanted to show is that even in these circumstances, there is an abnormal response to vasopressin.