Background
In observational studies, increased water intake improves kidney function but not in adults with chronic kidney disease (CKD) stage 3 and more and strongly depends on renal functional reserve (RFR) [1–3]. The CKD WIT trial has shown a nonsignificant gradual decline in kidney function after 1 year of coaching to increase water intake (CIWI) [3]. The CIWI (Early Coaching to Increase Water Intake in CKD — ECIWIC trial) benefits in CKD stage 1–2 (G1, G2) depends on RFR [4]. A recent study has shown that in patients with CKD, the relation between plain water intake and progression to kidney failure appears to be U-shaped; both low and high intake may not be beneficial in CKD [5].

The parallel-group randomized trial was aimed to determine the effect of CIWI on estimated glomerular filtration rate (eGFR) and RFR in adults with CKD stage 3 and CKD stages 4–5.

Coaching to increase water intake in CKD 1–5: overview and detailed analysis of three clinical trials

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Abstract. Parallel two-group prospective multicentre randomized trial named “HYD45 — Hydration in CKD 4–5 stages” that enrolled 62 patients with CKD G4–5 was aimed at evaluating of estimated glomerular filtration rate (eGFR) with coaching to increase water intake (CIWI) with the achievement of minimally higher diuresis by 400 mL in 31 patients compared with the CKD G4–5 group without CIWI. The stated duration was 12 months, and the trial was terminated in 6 months due to a more pronounced eGFR drop in the CIWI group, namely ~3.3 ml vs. 2 ml in the group without CIWI. EFR, renal functional reserve (RFR), albumin-to-creatinine ratio, and patient’s quality of life were additionally analyzed in this trial. Finally, three randomized clinical trials were analyzed in which patients with CKD 1–2, 3, and 4–5 received hydration. The results of studies demonstrate the possible efficacy of CIWI in stage 1–2 CKD in patients with normal or increased renal functional reserve. In stage 3 CKD, CIWI showed no benefits, and in stage CKD 4–5, forced hydration resulted in greater renal function loss. Summarizing these data, the authors concluded that it is probably appropriate for healthy people to consume the amount of fluid that provides physiological diuresis of 1.2–1.8 L and urine normal osmolarity. CIWI is often excessive, forced excessive hydration may not promote a healthy lifestyle. CIWI becomes forced excess hydration as kidney function decreases. Possibly, the benefits of CIWI are lost in CKD with the progression of renal function reduction. The effect of CIWI for 12 months may be positive for stage 1 CKD and stage 2 CKD with normal functional renal reserve. CIWI is probably impractical for chronic stages 3–5 CKD. In CKD 4–5, RFR is not preserved, which probably explains the negative effect of CIWI. With CKD G1, the CIWI leads to the optimal preservation of the renal function with the increase of GFR per 1 ml/min/1.73 m² per year in comparison with the same water intake. In CKD G2, CIWI prevents physiological and pathological loss of renal function, RFR above 50 % provides restoration of eGFR in CKD G1–2. Early Coaching to Increase Water Intake in CKD (ECIWIC) trial demonstrates benefits of CIWI in patients with CKD G1–2 and preserved RFR and may be recommended to delay the CKD worsening.

Keywords: early coaching to increase water intake in CKD; eGFR; renal functional reserve

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Materials and methods

We analyzed the data of CKD WIT, CKD-REIN [3, 5], and ECIWIC [4] trials for CKD 1–2, adding the data of a randomized clinical parallel-group trial of CKD WIT conducted in patients with CKD G3 and HYD45 conducted in patients with CKD G4–5 during 12 months. All patients at each stage were divided into two groups: 1) coaching to increase water intake, 2) coaching to maintain water intake. The primary outcome was the change in kidney function by eGFR from baseline to 12 months. The secondary outcome was a 1-year change in urine RFR. The subjective assessment of the quality of health (QH) has been estimated.

Results and discussion

CIWI may help preserve renal function loss and decline of eGFR in CKD G1 and G2 but isn’t beneficial in CKD G3–5 [3–5] (Fig. 1).

Of 124 patients randomized (mean age 53.2 years; men 83 (67%)), no one died; mean change in 24-hour urine volume was 0.6 L per day in CKD G1 group with CIWI and 0.5 L in G2.

No statistically significant data on eGFR depending on CIWI were obtained (Table 1). However, the trend suggests that CIWI improves eGFR in CKD G1 (from 95 to 96 ml/min/1.73 m²) and preserves eGFR decline in CKD G2 (78–78). Although coaching to maintain the same water intake didn’t preserve physiological and pathological eGFR decreasing in CKD G1–2 (G1 from 96 to 93, G2 from 76 to 73; t = 0.6; p = 0.29; P ≤ 0.05 for all groups).

An individual analysis of the RFR has shown that patients with RFR more than 50% (G1 — 19 patients (61%), G2 — 13 patients (42%)) had reliable preservation of eGFR with its increase of 1.5 ml/min/1.73 m² on CIWI, while patients with low functional renal reserve had a drop of eGFR at 1.1 ml/min/1.73 m² within 12 months. Patients with low normal serum sodium levels have shown worse results on CIWI.

The reduction of albumin-to-creatinine ratio does not depend on the eGFR but strongly correlates with RFR (CC 0.81). Patient-reported overall QH has been insignificantly higher in CIWI groups.

The randomized clinical parallel-group trial CKD WIT for CKD stage 3 analyzed 631 patients. Our randomized

| Intervention | CKD stage |
|--------------|-----------|
|              | CKD G1, n = 62 | CKD G2, n = 62 | CKD G3, n = 631 | CKD G4–5, n = 62 | RR G1-G5 |
| With CIWI    | +1.2       | 0              | −2.2             | −3.3              | 1.419    |
|              | (95% CI 0.619–3.255, NNT 9.5) |
| Without CIWI | −3.0       | −3.2           | −1.9             | −2.1              | 0.341    |
|              | (95% CI 0.136–0.854, NNT 5.0) |

Figure 1. The effectiveness of CIWI in CKD G1 and G2

Table 1. Changes in eGFR in CKD 1–5 (ml/min/1.73 m²)
clinical parallel-group trial HYD45 for CKD stage 4–5 enrolled a total of 62 patients (mean age 55.1 years; 35 men (58 %)); mean change in 24-hour urine volume was 0.6 L per day in the G3 group, 0.4 L per day in G4 with CIWI and 0.3 L in G5.

Mean change in eGFR in CKD G3 was –2.2 mL/min/1.73 m² in the hydration group and –1.9 mL/min/1.73 m² in the control group (adjusted difference between the groups –0.3 mL/min/1.73 m² [95% CI –1.8 to 1.2; p = 0.74]). No statistically significant data on eGFR change in CKD 4–5 depending on CIWI was obtained. However, in the HYD45 trial we had to terminate the study in 6 months due to a more pronounced drop of eGFR in the CIWI group, namely: –3.3 mL vs. 2 mL in the group without CIWI. RFR was 12 % in CKD G3, 6 % in CKD G4, and negative in CKD G5.

The data of our analysis are presented in Table 1.

The data obtained correlates with the results of a recently published study [6] (Fig. 2).

In any case, patients with CKD should be careful about water load, commensurate with the magnitude of the glomerular filtration rate.

Conclusions

1. Proper recommendations are the coaching to increase water intake that provides physiological diuresis of 1.2–1.8 L and normal urine osmolality.

2. CIWI is a healthy option, especially for common healthy people with normal renal function.

3. CIWI is healthy and advisable for people with CKD stage 1–2.

4. CIWI loses its benefits with a decrease of renal function from CKD stage 3 to 4 and probably becomes inadvisable in CKD stage 5.

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Примусовая гидратация при ХХН стадий 1–5: обзор и детальный анализ трех клинических исследований

Резюме. Параллельное в 2 группах проспективное многоцентровое национальное исследование, проведенное под названием «HYD45 — Гидратация при 4–5-й стадии ХХН», проведено в 62 пациентах из ХХН G4–5, было оценено рандомизированной швейцарской клинико-фармацевтической древности (рШКФ) и выполнен при принудительной гидратации (CIWI) с достижением более высокого диуреза минимально на 400 мл у 31 пациента из группы с ХХН G4–5 без CIWI. Защитная продолжительность исследования составила 12 месяцев, исследование было прекращено через 6 месяцев из-за менее выраженного падения рШКФ в группе CIWI, а именно: 3,3 мл/сут на 2 мл с тем же потреблением воды. В этом исследовании дополнительно анализировались рШКФ, почечный функциональный резерв нирок (ФНР), спонтанное диуреза и кровотечения. При ХХН G2 CIWI предотвращает восстановление рШКФ при ХХН G1–2, что может быть связано с нормальной функцией почек, восстанавливаясь и сохраняя рШКФ. Результаты исследования указывают на возможную эффективность CIWI при 1–2-й стадии ХХН, которая встречается у пациентов с нормальным или повышенным функциональным резервом почек. На стадии 3 ХХН CIWI не показала положительных результатов, а на медикаментозной стадии 4–5 CIWI принудительная гидратация приводила к большей потере функции почек. Обобщая эти данные, авторы пришли к выводу, что здоровыми людям, возможно, целесообразно потреблять такое количество жидкости, которое обеспечивает физиологический диурез 1,2–1,8 л и нормоосмолярность почек. CIWI часто включается в клинические исследования, однако рекомендуется применять гидратацию для борьбы с хроническими заболеваниями почек.

Ключевые слова: хроническая холестерозная нирка, хроническая холестерозная нирка, CIWI, гидратация, рШКФ, ФНР, ФПР, гидратация, физиологический диурез.

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