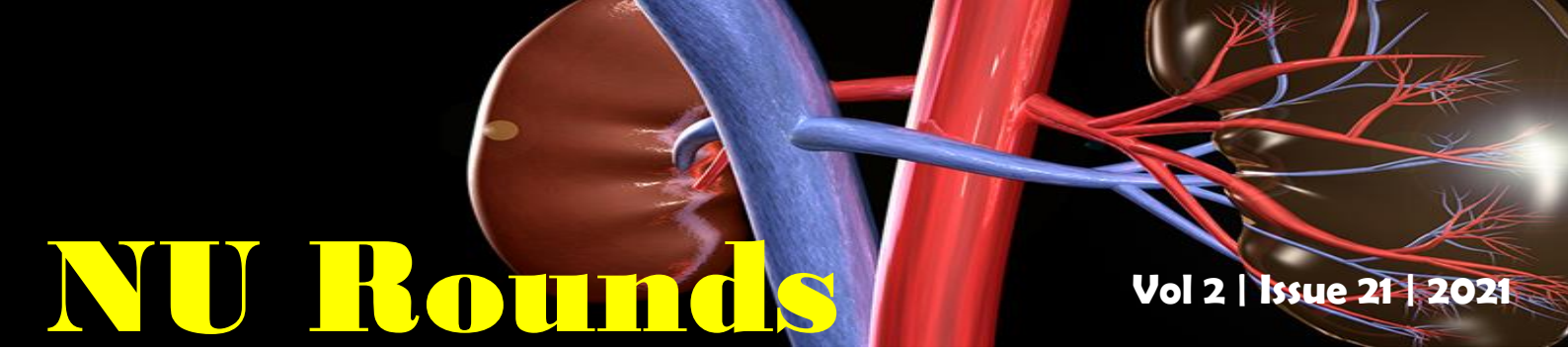

NU Rounds

Vol 2 | Issue 21 | 2021

Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you "**NU Rounds**" which contains latest and interesting news in the field of Urology.

Inside This Issue:

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

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Desmopressin versus desmopressin + oxybutynin in the treatment of children with nocturnal enuresis

Introduction

Enuresis is identified as voluntary or involuntary leakage of urine for at least three consecutive months in the daytime and/or night-time on clothes for children older than five. Monosymptomatic nocturnal enuresis (MNE) describes night-time wetting without daytime leakage of urine in children with no pathology in the urinary system and it is 80% more common than enuresis. Desmopressin is the most common medical treatment for MNE.

Aim:

Retrospectively compare the effectiveness of desmopressin as monotherapy and desmopressin + oxybutynin as a combination therapy in the treatment of nocturnal enuresis.

Material and Method

Retrospectively evaluation of 183 patients who applied to pediatrics, pediatrics surgery and urology clinics with the complaint of nocturnal enuresis and diagnosed with primary monosymptomatic nocturnal enuresis between January 2014 and December 2019. Patients were divided into two groups: (91 patients) who only received desmopressin therapy (Group 1), and those (92 patients) who received desmopressin and oxybutynin combination therapy (Group 2).

Outcomes:

- Response to treatment, compliance and recurrence ratios were determined in the evaluation.

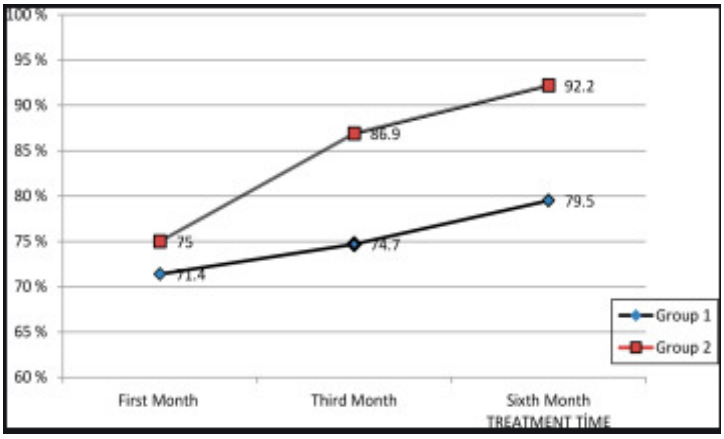
Response:

- Complete response was accepted as 90-100% decrease in the number of nighttime wetting,

- Partial response was accepted as 50-90% decrease in the number of nighttime wetting
- Below 50% were regarded as non-response.
- The 1st, 3rd, and 6th months of control data of treatment effectiveness of both groups were evaluated and their responses to treatment and the side effects of drugs were examined.

Results

The mean age 183 patients of whom 103 were male and 80 were female was 10 (6-16) year. In the first month of control of Group 1, 71.4% had a complete cure, 8.8% had a partial cure and 19.8% had no response to treatment. In the third month of control of Group 1, 74.73% gave a complete response and were cured, 5.5% gave a partial response and 19.78% had no response. In the sixth month of Group 1, 70 patients were evaluated as complete response (79.5%), and 5 patients were evaluated as partial response (5.6%).



In the first month of control of Group 2, 75% gave a complete response, 10.9% gave a partial response, 14.1% had no response to treatment. In the third month of control of Group 2, 86.9% gave a complete response, 6.52% gave a partial response, and 6.52% had no response. In the sixth month of the control of Group 2, the number of patients who did not come for control and could not be reached was 2, 83 patients out of 90 patients were evaluated as complete response (92.2%), 6 patients were evaluated as partial response (6.6%).

Conclusion

Desmopressin is the only FDA approved pharmacologic treatment for nocturnal enuresis. Desmopressin reduces urine production and the anticholinergic agent allows the bladder to

store more urine. Therefore, combined therapy can be recommended in the MNE treatment for specially selected cases.

Source: Gozukucuk A, et al. Desmopressin versus desmopressin + oxybutynin in the treatment of children with nocturnal enuresis. Journal of Pediatric Urology. 2021 April.

Xanthogranulomatous pyelonephritis: a focus on microbiological and antibiotic resistance profiles

Introduction:

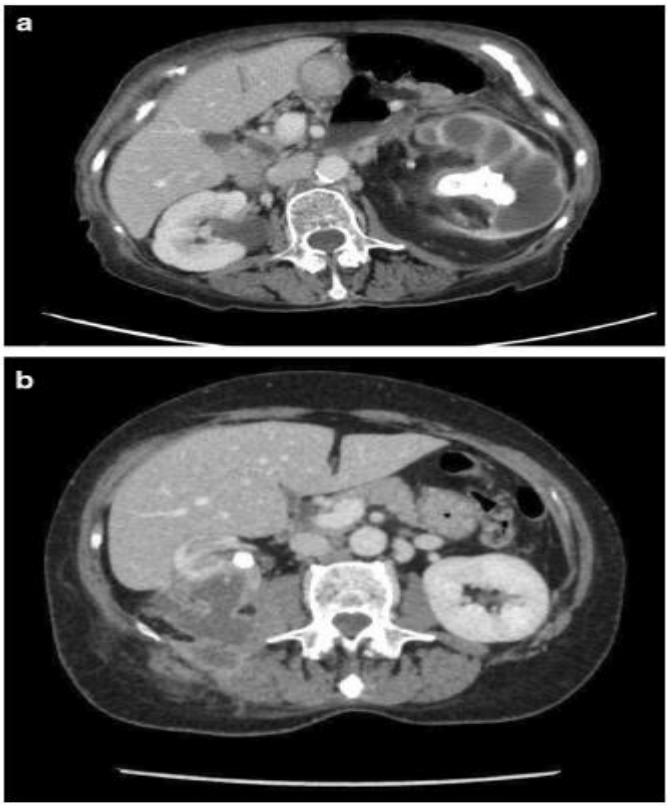
Xanthogranulomatous pyelonephritis (XGP) is a chronic granulomatous inflammation characterized by destruction of the renal parenchyma and replacement by solid sheets of lipid-laden macrophages. This rare entity constitutes less than 1% of chronic pyelonephritis. *Escherichia coli* and *Proteus mirabilis* are the isolated agents in approximately 90% of positive urinary cultures of XGP patients, although sterile urine cultures are not uncommon. Generally, treatment of XGP includes antibiotic therapy and drainage of the abscess followed by nephrectomy for definitive treatment. Total nephrectomy (or in rare circumstances of focal XGP, partial nephrectomy) is the treatment of choice, and it is usually technically difficult due to extensive kidney adhesions to surrounding structures. Although surgery is regarded as the gold standard, antibiotic treatments have been proposed in children with unusual bilateral and focal XGP (with functioning kidney). In addition, symptomatic management through percutaneous drainage of abscesses can contribute to successful initial management of XGP. Because XGP symptoms can be nonspecific, a diagnosis is often delayed, so imaging studies (ultrasound scan and computed tomography) are important in patients with recurrent or persistent pyelonephritis despite having been treated with adequate antibiotic therapy.

Methods: A retrospective study of 27 cases of XGP diagnosed between January 2001 and January 2020 to analyse their clinical and management characteristics. In addition, a literature review was conducted of XGP case series covering the period from 2000–2020. Studies

reporting case series of XGP (more than ten cases) were included if they were relevant to this study.

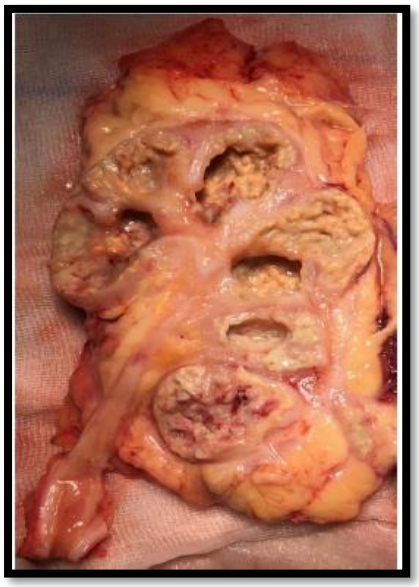
Results: Twenty-seven patients were diagnosed with XGP, and 26 of them were histologically proven to have XGP. A total of 81.5% of the patients were female and the mean age was 59.6 years (SD 19.2).

Axial CT scan images demonstrate obstructing left pelvic staghorn stone with associated grade IV hydronephrosis (Malek I) (a) and retroperitoneal collections surrounding the right kidney with a renal pelvic calculus (Malek III) (b)



The most frequent symptoms were flank pain (70.4%) and fever (59.3%), while 77.8% of patients had renal stones. *Proteus mirabilis* was detected in the urine culture in 18.5% of patients, followed by detection of *Escherichia coli* in 14.8% of patients.

Gross examination shows enlarged kidney and yellow nodules in the renal parenchyma



The computed tomography (CT) findings included perirenal (29.6%) or pararenal (29.6%) involvement in the majority of patients. Twenty-six patients underwent nephrectomy. Piperacillin/tazobactam and ceftriaxone were the most commonly prescribed antibiotics for treatment. The reported piperacillin/tazobactam and ceftriaxone resistance rates were 14.3% and 16.6%, respectively. Twenty-six case series were included in the literature review, reporting 693 cases in total.

Conclusion:

Well-established characteristics of XGP patients among series in terms of previous history, clinical, laboratory and imaging findings, and operative and postoperative outcomes. It is important to know the clinical presentation and potential severity of XGP, as well as the most frequently involved microorganisms and their antibiotic resistance profiles, to select the most appropriate antibiotic therapy.

Source: Artiles-Medina A, et al. Xanthogranulomatous pyelonephritis: a focus on microbiological and antibiotic resistance profiles. BMC Urol. 2021 Apr 7;21(1):56.

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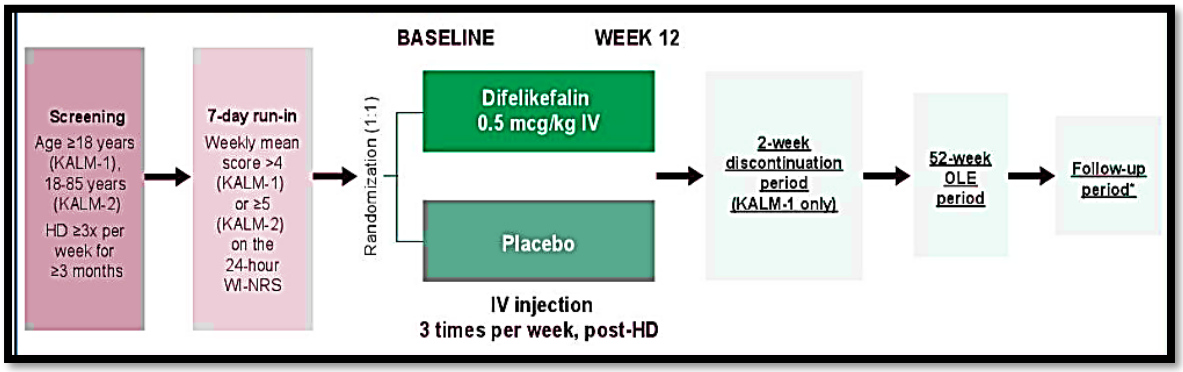
Long-term Safety and Efficacy of Difelikefalin in Patients With Chronic Kidney Disease–Associated Pruritus: Analysis From KALM-1 and KALM-2

Introduction

Difelikefalin (DFK) is a novel, selective kappa-opioid receptor (KOR) agonist with minimal central nervous system penetration. It does not bind to mu-opioid receptors or any known receptors other than KORs1. The antipruritic effect is thought to occur via activation of KORs located on peripheral sensory neurons and immune cells. In the phase 3 KALM-1 and KALM-2 studies of intravenous (IV) DFK in patients with moderate-to severe chronic kidney disease–associated pruritus (CKD-aP) undergoing hemodialysis, DFK showed significant improvements in itch-related quality of life (QoL) vs placebo at week 12 and an acceptable safety profile. We report long-term QoL and pooled safety data from the placebo-controlled and open-label extension (OLE) periods of the KALM-1 (NCT03422653) and KALM-2 (NCT03636269) phase 3 studies

Methods: KALM-1 and KALM-2 were randomized, phase 3, multicenter, placebo-controlled studies.

KALM-1 and KALM-2 Study Designs



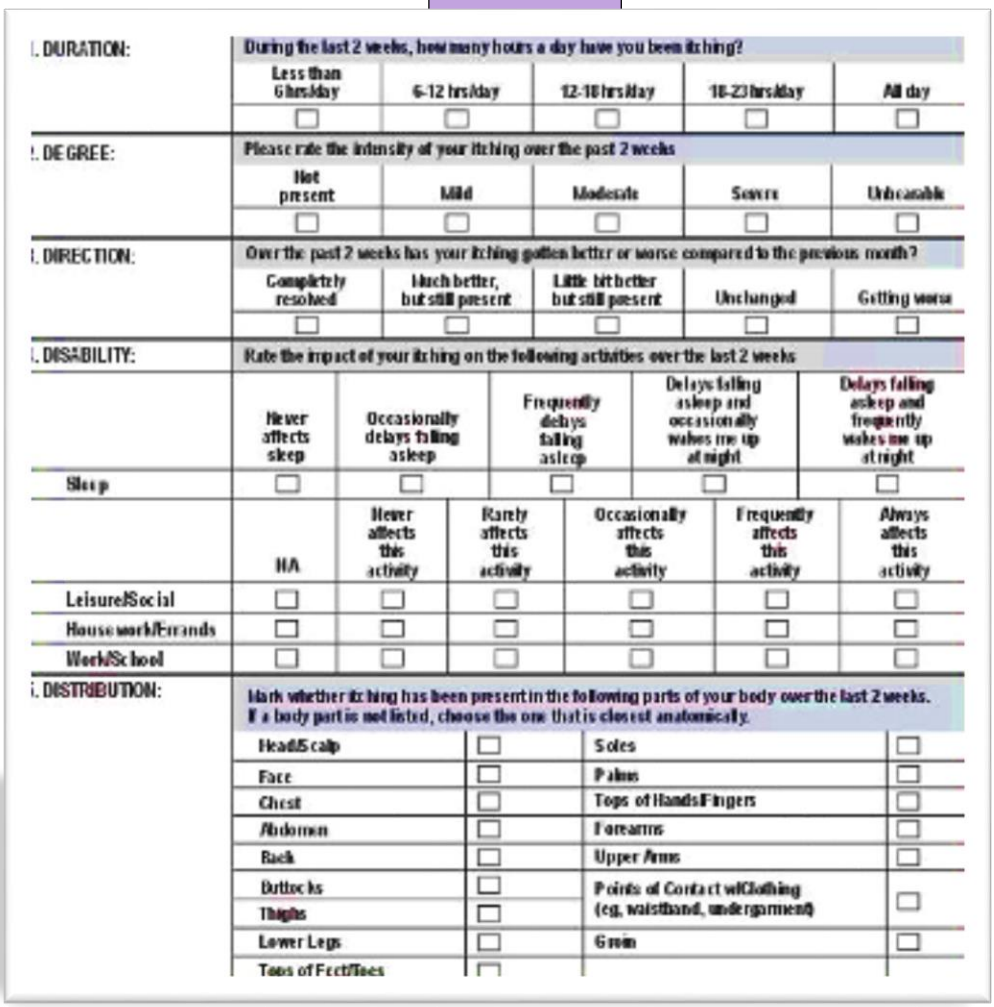
KALM-1 was conducted in the United States, and KALM-2 was conducted in the United States, Europe, Asia, Australia, Canada, and New Zealand. Patients with moderate-to-severe

CKD-aP undergoing hemodialysis were randomized to IV DFK 0.5 mcg/kg or placebo 3 times/week for 12 weeks, followed by a ≤ 52-week OLE in which all patients received IV DFK 0.5 mcg/kg 3 times/week

Outcomes

Itch-related QoL: Assessed with the 5-D Itch scale. The 5-D Itch scale assesses 5 dimensions of itch (duration, degree, direction, disability, and distribution) during a 2-week recall period. The 5-D Itch scale ranges from 5 to 25, with higher scores indicating worse itch-related QoL. Safety: Evaluated based on adverse events (AEs), physical examinations, vital signs, electrocardiograms, and clinical laboratory tests.

5D Itch Scale



DURATION:	During the last 2 weeks, how many hours a day have you been itching?				
	Less than 6 hrs/day	6-12 hrs/day	12-18 hrs/day	18-23 hrs/day	All day
	☐	☐	☐	☐	☐
DEGREE:	Please rate the intensity of your itching over the past 2 weeks				
	Not present	Mild	Moderate	Severe	Unbearable
	☐	☐	☐	☐	☐
DIRECTION:	Over the past 2 weeks has your itching gotten better or worse compared to the previous month?				
	Completely resolved	Much better, but still present	Little bit better but still present	Unchanged	Getting worse
	☐	☐	☐	☐	☐
DISABILITY:	Rate the impact of your itching on the following activities over the last 2 weeks				
	Never affects sleep	Occasionally delays falling asleep	Frequently delays falling asleep	Delays falling asleep and occasionally wakes me up at night	Delays falling asleep and frequently wakes me up at night
Sleep	☐	☐	☐	☐	☐
	NA	Never affects this activity	Rarely affects this activity	Occasionally affects this activity	Frequently affects this activity	Always affects this activity
Leisure/Social	☐	☐	☐	☐	☐	☐
Housework/Errands	☐	☐	☐	☐	☐	☐
Work/School	☐	☐	☐	☐	☐	☐

DISTRIBUTION:	Mark whether itching has been present in the following parts of your body over the last 2 weeks. If a body part is not listed, choose the one that is closest anatomically.		
Head/Scalp	☐	Soles	☐
Face	☐	Palms	☐
Chest	☐	Tops of Hands/Fingers	☐
Abdomen	☐	Forearms	☐
Back	☐	Upper Arms	☐
Buttocks	☐	Points of Contact w/Clothing (eg, waistband, undergarment)	☐
Thighs	☐		
Lower Legs	☐	Groin	☐
Toes of Feet/Toes	☐		

Results:

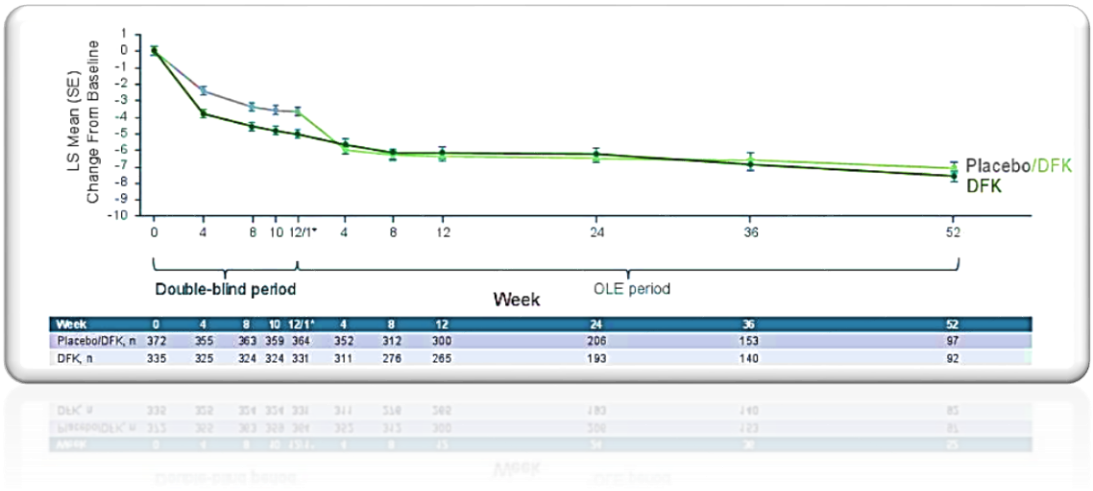
- The pooled KALM-1 and KALM-2 population included 851 patients (DFK: 426; placebo: 425); 340 DFK patients and 372 placebo patients entered the OLE
- In KALM-1, 378 patients were randomized (DFK: 189; placebo: 189)
- In KALM-2, 473 patients were randomized (DFK: 237; placebo: 236)
- In the pooled KALM-1 and KALM-2 population, there were 796 patients exposed to DFK in either the placebo-controlled period or the OLE
- There were 84 patients from the placebo controlled period who were not included in the OLE because they were not eligible or chose not to enter the OLE

Safety

- In the pooled studies, patients reported treatment-emergent AEs (TEAEs; Table 2) that were mostly mild to moderate in the placebo-controlled period (DFK: 57.5% [244/424]; placebo: 52.6% [223/424]) and the OLE period (DFK: 53.6% [427/796])
- The incidence rate of AEs leading to death through ≤64 weeks of treatment was within the reported rate in HD patients from the United States Renal Data System (USRDS) – USRDS unadjusted incidence of death in HD patients: 164.6/1,000 pt-yrs
- Incidence rates of common AEs in the placebo-controlled period did not increase in the OLE period

Itch-Related QoL

Mean 5-D Itch improvement with DFK was maintained through the 52-week OLE with continued DFK treatment and emerged in patients who switched from placebo to DFK during the OLE



Week	0	4	8	10	12/1*	4	8	12	24	36	52
Placebo/DFK, n	372	355	363	359	364	352	312	300	206	153	97
DFK, n	335	325	324	324	331	311	276	265	193	140	92

Conclusions:

- DFK demonstrated maintenance of efficacy over 1 year in itch related symptoms and QoL
- IV DFK 0.5 mcg/kg was well tolerated with an acceptable long-term safety profile in patients with CKD-aP undergoing HD. TEAEs were mostly mild to moderate in severity
- The incidence rate of common TEAEs and serious TEAEs did not increase with longer term exposure The incidence of death in the pooled studies was lower than the unadjusted incidence of death reported for patients undergoing HD in the USRDS 2020 annual report
- These findings suggest that DFK may help to address the unmet need for treatments that are well tolerated and efficacious over the long term for moderate-to-severe CKD-aP in patients undergoing HD

Source: Fishbane S. Long-term Safety and Efficacy of Difelikefalin in Patients With Chronic Kidney Disease–Associated Pruritus: Analysis From KALM-1 and KALM-2. Presented at: the National Kidney Foundation 2021 Spring Clinical Meetings, April 6–10, 2021.