Ursodiol in Patients with Parenteral Nutrition–Associated Cholestasis

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OBJECTIVE: To review the role of ursodeoxycholic acid (ursodiol) in treating parenteral nutrition–associated cholestasis (PNAC).

DATA SOURCES: A MEDLINE (1950–May 2007) search was performed using the key terms parenteral nutrition, cholestasis, ursodeoxycholic acid, and ursodiol.

STUDY SELECTION AND DATA EXTRACTION: All English-language articles that evaluated the safety and efficacy of ursodiol for PNAC were included in this review.

DATA SYNTHESIS: The benefits of exogenous ursodiol administration in the treatment of cholestasis can be explained by its alteration of effects on bile composition and flow and provision of cytoprotective, membrane stabilizing, and immunomodulatory effects. Two animal studies, 2 case reports, and 6 human studies (2 prospective and 3 retrospective pediatric studies, 1 adult prospective study) evaluated the efficacy of ursodiol in patients with PNAC. Ursodiol 10–30 mg/kg/day in children and 10–15 mg/kg/day in adults administered in 2–3 doses improved the biochemical and clinical signs and symptoms of PNAC. However, short-term improvement in biochemical parameters may not necessarily predict the outcome of PNAC patients. At recommended doses, ursodiol may not be effective in patients with short bowel syndrome or in those with resected terminal ileum because of reduced ursodiol absorption. Studies supporting the efficacy of ursodiol in treatment of PNAC are limited by small sample size, absence of randomization and controls, short duration, and lack of accountancy to confounding variables. Large, prospective, randomized, placebo-controlled, long-term follow-up studies evaluating the efficacy and optimal dosing and duration of ursodiol therapy for PNAC are not yet available.

CONCLUSIONS: Ursodiol may improve the biochemical signs and clinical symptoms of PNAC. However, optimal dosing, timing, duration of therapy, and long-term effects on PNAC outcome and prognosis require further studies.

KEY WORDS: cholestasis, parenteral nutrition, ursodeoxycholic acid, ursodiol.

Ann Pharmacother 2007;41:1867-72.

Published Online, 2 Oct 2007, *www.theannals.com*, DOI 10.1345/aph.1K229

Request

Is ursodeoxycholic acid (ursodiol) effective for the treatment of parenteral nutrition–associated cholestasis (PNAC)?

Response

BACKGROUND

Parenteral nutrition is indicated in malnourished patients and in those at risk for malnutrition when feeding into the gastrointestinal tract is contraindicated or inadequate. Parenteral nutrition can be associated with liver toxicities including cholestasis, steatosis, and cholelithiasis. PNAC is the most common and complex liver toxicity in parenteral nutrition–dependent patients. Elevated serum conjugated bilirubin and γ-glutamyl transpeptidase (GGT) concentrations are indicators of PNAC. Serum conjugated bilirubin better reflects bile flow, and concentrations of 2–2.5 mg/dL or greater (normal <0.3 mg/dL) are the most specific and sensitive biochemical markers of PNAC. Short-term improvement in liver biochemical parameters, except possibly for serum conjugated bilirubin concentrations, may not predict the long-term outcome of patients with PNAC.[1,2] Long-term follow-up of serum conjugated bilirubin concentrations for the duration of parenteral nutrition is essential.

This article reviews the literature related to ursodiol's role in patients with PNAC.

Predisposing factors to PNAC include premature birth, parenteral nutrition dependence, overfeeding, lack of enteral feeding, short bowel syndrome, and sepsis.[3] Prolonged bowel rest causes decrease in gut immunity and integrity, promotes intestinal bacterial overgrowth, and causes decreased cholecystokinin (CCK) secretion in the duodenum leading to diminished gallbladder contractility and bile stasis.[4] Initiation of oral or enteral feedings is essential to restore gut functionality and minimize or prevent PNAC.

Author information provided at the end of the text.

Pharmacologic agents used to enhance bile flow are cholecystokinin–octapeptide (CCK-OP, sincalide) and ursodiol.[3] Although CCK-OP improves the signs and symptoms of PNAC, a prospective multicenter study in children showed that CCK-OP failed to prevent PNAC.[5] Ursodiol is used in the treatment of hepatic disease with defective biliary secretion, but studies of the drug's use in treatment of PNAC are limited.[6-11] In a study of oral tauroursodeoxycholic acid (tursodiol), a conjugate of ursodiol, using doses of 30 mg/kg/day, low birth weight infants did not achieve significant ursodiol bile enrichment and PNAC was not prevented.[12] Currently, there is one clinical trial evaluating the role of tursodiol for prevention and treatment of PNAC.[13]

Ursodiol is a hydrophilic bile acid that constitutes 1–3% of bile acids. Once expelled from the gallbladder, ursodiol is solubilized in mixed micelles in the jejunum and is thereafter 90% absorbed throughout the small bowel, mainly in the terminal ileum. Ursodiol undergoes enterohepatic recycling and is conjugated in the liver with glycine or taurine; it is subsequently secreted into the bile.[4] Like all bile acids, ursodiol absorption is limited in patients with short-bowel syndrome because of limited intestinal area or function.[14] Several mechanisms are proposed for ursodiol actions including correcting bile acid deficiency, improving bile flow, displacing cytotoxic bile acids (cholic and lithocholic acids), and providing cytoprotective, membrane-stabilizing, and immunomodulatory effects.[3,14-18] Ursodiol dosing in adults is 13–15 mg/kg/day in 4 divided doses for primary biliary cirrhosis, 8–10 mg/kg/day in 2–3 divided doses for gallstone dissolution, and 300 mg twice daily for gallstone prevention. Although not approved for pediatric use, ursodiol 30 mg/kg/day in 3 divided doses is used in children with PNAC.[19]

The drug is available only in oral dosage forms with the following average wholesale prices per dose: Actigall 300 mg capsule ($4.37), Urso 250 250 mg tablet ($2.35), Urso Forte 500 mg tablet ($4.27), and generic ursodiol 300 mg tablet ($2.57).[20] Oral suspensions of 20, 25, 50, and 60 mg/mL are extemporaneously prepared.[19] An extemporaneous oral suspension of 25 mg/mL can be prepared by levigating the contents of ten 300 mg capsules with 10 mL of glycerin and adding 60 mL of Ora-Plus. Orange syrup is added to obtain a total volume of 120 mL.[21]

LITERATURE REVIEW

MEDLINE (1950–March 2007) was searched using the terms parenteral nutrition, cholestasis, ursodeoxycholic acid, and ursodiol. All relevant articles published in English were identified, evaluated, and included in this review. Two animal studies, 2 case reports (1 in children, 1 in adults), and 6 human studies (2 prospective and 3 retrospective in pediatrics, 1 prospective in adults) that evaluated ursodiol's role in PNAC patients were identified. A summary of clinical studies is in Table 1.

Animal Studies

Studies in animals with induced PNAC showed that ursodiol improves bile flow and normalizes liver function tests.[22,23] Adding metronidazole to ursodiol therapy further decreased serum bilirubin concentrations and prevented parenteral nutrition–associated liver histological abnormalities.[23]

Case Reports

A case report described a parenteral nutrition–dependent infant with short-bowel syndrome (10 cm of jejunum and 7 cm of terminal ileum remaining) with an elevated serum bilirubin concentration (7.5 mg/dL).[24] Ursodiol was initiated at 18.5 mg/kg/day and increased to 35 mg/kg/day in 3 divided doses, which resulted in resolution of hyperbilirubinemia. Because hyperbilirubinemia coincided with catheter-related bloodstream infections, the effect of sepsis on increasing bilirubin could not be excluded. Also, the extent of ursodiol absorption to achieve therapeutic effects is questionable with the very short small bowel length. However, the use of a high ursodiol dose and the remaining 7 cm of distal ileum, which is the main site of bile acid absorption, may have compensated for malabsorption.

Another case report of a 52-year-old parenteral nutrition–dependent patient with 66 cm of jejunal resection described the role of ursodiol in PNAC.[25] Despite adjusting parenteral nutrition calories and treatment with oral metronidazole, the serum bilirubin concentration remained elevated at 14.8 mg/dL. Metronidazole was discontinued and ursodiol was started at 300 mg twice daily. Within 3 weeks of ursodiol therapy, serum bilirubin concentrations decreased to 8.4 mg/dL, then to 2 mg/dL 2 months later, and ultimately dropped to 1 mg/dL with resolution of pruritus. Serum bilirubin concentration rebounded to 4 mg/dL following ursodiol discontinuation but normalized after ursodiol was restarted.

Clinical Studies

A pilot study evaluated the effects of ursodiol for treating PNAC in 7 parenteral nutrition–dependent children with protracted diarrhea.[6] Diagnosis of PNAC was established by elevated serum GGT, alkaline phosphatase (ALP), and aminotransferase concentrations with or without conjugated hyperbilirubinemia. All patients had elevated serum GGT concentrations (range 200–700 IU/L), 5 patients had elevated serum conjugated bilirubin concentrations (2–8 mg/dL), 5 had jaundice and hepatomegaly, and 6 had splenomegaly. Normal serum albumin concentrations were observed in all children. Cholestasis occurred for 15–560 days before ursodiol was started. Ursodiol 30 mg/kg/day was administered in 3 divided doses (duration 48–575 days, median 294) and resulted in resolution of jaundice and hepatosplenomegaly within 1–2

Table 1. Clinical Studies of Ursodiol Use in Treatment of Parenteral Nutrition–Associated Cholestasis

Reference	Design	Population	UDCA Dose (mg/kg/day)	Outcomes Measured	Results	Comments
Beau (1994)[11]	P, NR	SBS adults with PNAC (N = 9)	10–15	serum total bilirubin, ALP, ALT, AST, and GGT concentrations	significant reduction from baseline in serum GGT (27.1% and 20.4%, respectively; p = 0.001) and ALT (7% and 34.8%, respectively; p = 0.01) concentrations; no significant decrease in serum AST, ALP, and total bilirubin concentrations; washout periods associated with rebound in serum GGT, ALT, and ALP concentrations; diarrhea reported in 2 pts. (remaining small bowel length 5 cm and 20 cm) prompting UDCA dose reduction to 6 mg/kg/day in 1 pt. (residual small bowel length 20 cm)	all pts. allowed oral nutrition, which also prevents PNAC
Spagnuolo (1996)[6]	P, observational	PN-dependent children with protracted diarrhea and PNAC (N = 7)	30	serum ALP, ALT, GGT, and conjugated bilirubin concentrations	resolution of jaundice and hepatosplenomegaly within 1–2 wk; normalization of serum GGT, ALP, ALT in 4–8 wk; resolution of hyperbilirubinemia within 3–6 wk	serum GGT concentrations remained elevated in pt. with longest duration of cholestasis (560 days) before UDCA was started
Levine (1999)[8]	R	premature infants with PNAC (N = 6); gestational age (mean ± SD) 29.8 ± 4.2 wk	15–30	serum total and conjugated bilirubin, ALP, ALT, and AST concentrations	steady but insignificant decrease of serum total and conjugated bilirubin, ALT, AST, and ALP concentrations within 2 wk of therapy	no dose–effect comparisons between dosing regimens; all infants received enteral feedings
Chen (2004)[9]	R	VLBW infants with PNAC; treatment group gestational age (mean ± SEM) 27.5 ± 0.5 wk, n = 12; control group gestational age 28.4 ± 0.7 wk, n = 18	10–30	serum total and conjugated bilirubin, AST, ALT, ALP, and GGT concentrations	significantly shorter duration of cholestasis in treatment vs control group (62.8 ± 10.7 vs 92.4 ± 8.8 days; p = 0.006); significantly lower peak serum total and conjugated bilirubin concentrations in treatment group vs control group (peak total bilirubin 8.8 ± 1.6 mg/dL and 13.9 ± 1.7 mg/dL, respectively; p = 0.007; peak direct bilirubin 5.3 ± 0.6 mg/dL and 8.7 ± 1.1 mg/dL, respectively; p = 0.023); no significant effect on peak serum AST, ALT, GGT, or ALP concentrations	no dose–effect comparison between dosing regimens; enteral feedings were gradually advanced; age to tolerate full enteral feedings not significantly different between groups
Al-Hatholol (2006)[10]	R	surgical VLBW infants with PNAC (N = 13); mean ± SEM gestational age 29.3 ± 1 wk	15–20	serum total and conjugated bilirubin, ALP, ALT, AST, and GGT concentrations	compared with baseline, significant reduction in serum total bilirubin (14.3 ± 2.2 mg/dL vs 0.94 ± 0.1 mg/dL; p = 0.0001) and conjugated bilirubin (11.8 ± 1.8 mg/dL vs 0.58 ± 0.1 mg/dL; p = 0.0001) and AST concentrations (185 ± 22 U/L vs 80 ± 14 U/L; p = 0.001); insignificant improvement of serum ALP, ALT, and GGT concentrations; mild diarrhea in 3 pts.	concomitant sepsis with hyperbilirubinemia in 4 pts., which could have caused PNAC
De Marco (2006)[7]	P, OL	SBS (n = 7) and functional SBS (n = 5) pediatric pts. with intestinal failure and PNAC	30	serum ALP, ALT, GGT, conjugated bilirubin, albumin, and UDCA concentrations	decrease in serum GGT, ALT, and direct bilirubin concentrations in both groups; no response and very low serum UDCA concentrations in 1 child with shortest small bowel length remaining; stopping UDCA caused rebound rise of serum GGT concentrations	effects of sepsis and concomitant enteral feedings on PNAC cannot be ruled out

ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; GGT = γ-glutamyl transpeptidase; NR = nonrandomized; OL = open-label; P = prospective; PN = parenteral nutrition; PNAC = parenteral nutrition–associated cholestasis; R = retrospective; SBS = short-bowel syndrome; UDCA = ursodeoxycholic acid; VLBW = very-low-birth weight.

weeks of therapy. In 6 patients, serum GGT, ALP, and alanine aminotransferase (ALT) concentrations normalized within 4–8 weeks. Serum GGT concentrations rebounded after ursodiol was stopped in 3 patients still on PN but normalized within 7–10 days after ursodiol was restarted.

The effects of ursodiol on PNAC were evaluated in 7 patients with short-bowel syndrome (residual small bowel length range 15–85 cm) and in 5 pediatric patients with intestinal failure due to primary intestinal diseases, also referred to as functional short-bowel syndrome.[7] Parenteral nutrition was initiated at a mean patient age of 11.1 months (range 0–134) for patients with short-bowel syndrome and 5.4 months (range 0–21) for patients with functional short-bowel syndrome. Mean duration of parenteral nutrition prior to onset of cholestasis was 1.9 months (range 0–5.4) and 4.2 months (range 1–13) for short-bowel syndrome and patients with functional short-bowel syndrome, respectively. Ursodiol 30 mg/kg/day was administered in 3 divided doses.

Compared with patients with functional short-bowel syndrome, those with short-bowel syndrome had a more rapid time-to-normalization of cholestasis (mean 2.1 mo, range 1–4 vs mean 3.3 mo, range 2–4) and time-to-response (mean 2 mo, range 1–2 vs mean 3.3 mo, range 2–5) respectively, but differences were not statistically significant. Stopping ursodiol in 4 patients (3 short-bowel syndrome, 1 functional short-bowel syndrome) after PNAC resolved was followed by rebound of serum GGT concentrations in 3 patients. Serum GGT concentrations returned to normal after ursodiol was reinitiated. Additionally, serum ursodiol concentrations were measured in 5 patients (4 short-bowel syndrome, 1 functional short-bowel syndrome) and values ranged widely (0.1–48 µmol/L). One patient with functional short-bowel syndrome and 3 patients with short-bowel syndrome with serum ursodiol concentrations of 48, 2.7, 5.2, and 34 µmol/L, respectively, responded to therapy. The patient with the shortest small bowel length (15 cm) and absent ileocecal valve had the lowest serum ursodiol concentration (0.1 µmol/L) and did not respond to therapy. Because ursodiol absorption can be significantly impaired in patients with very short remaining small bowel length, this may explain therapeutic failure in this patient. The study concluded that ursodiol 30 mg/kg/day is effective in children with short-bowel syndrome, and initiating ursodiol at the earliest sign of increased serum GGT concentrations improves the response. Although serum conjugated bilirubin concentrations decreased in patients with short-bowel syndrome following ursodiol therapy, they were not, used for the diagnosis of PNAC. Instead, serum GGT concentrations were considered the earliest and most sensitive markers of PNAC.[7]

A retrospective study evaluated the effects of ursodiol for the treatment of PNAC in 6 premature infants who received ursodiol for at least one month and had liver function evaluations weekly.[8] Increased serum conjugated bilirubin concentrations were the basis of PNAC diagnosis. Ursodiol 15–30 mg/kg/day was started (15 mg/kg/day in 2 infants, 20–25 mg/kg/day in 3 infants, 30 mg/kg/day in 1 infant) in 3 divided doses after a mean 9.5 ± 5.9 days of PNAC diagnosis. Serum total and conjugated bilirubin, ALT, aspartate aminotransferase (AST), and ALP concentrations steadily decreased through the first 2 weeks of therapy, but the difference did not reach statistical significance.

Ursodiol effects were also evaluated in a retrospective study of 30 very-low-birth weight (<1500 g) infants with PNAC (serum conjugated bilirubin concentrations >2 mg/dL).[9] Serum total and conjugated bilirubin, AST, ALT, ALP, and GGT concentrations were measured weekly during hospitalization, 2 weeks after discharge, and monthly thereafter until PNAC resolved. The treatment group included 12 patients treated with ursodiol; the remaining 18 patients were the control group. Initially, ursodiol 10–20 mg/kg/day was administered in 3 divided doses to the first 5 patients. In the absence of adverse effects, the ursodiol dose was increased to 30 mg/kg/day for the remaining 7 patients. Ursodiol was started after the onset of cholestasis at a mean of 6.4 ± 1.4 days for a mean duration of 51.5 ± 8.5 days. Results showed that ursodiol-treated patients had a significantly shorter mean duration of cholestasis compared with the control group. Peak serum total and conjugated bilirubin concentrations were significantly lower in the treatment group compared with the control group.[9]

Ursodiol effects were investigated in a study of 13 surgical very-low-birth weight infants with PNAC (serum conjugated bilirubin >2 mg/dL).[10] Cholestasis occurred at age 36.2 ± 2 days, and ursodiol was started at age 79 ± 6 days. Serum total bilirubin, conjugated bilirubin, ALP, ALT, AST, and GGT concentrations were measured prior to ursodiol therapy, weekly until ursodiol was stopped, and twice monthly for 3 months thereafter. Despite discontinuation of parenteral nutrition and full enteral feedings, serum conjugated bilirubin concentrations remained greater than 2 mg/dL. Ursodiol was not started until after parenteral nutrition had been stopped; the dose was 15–20 mg/kg/day in 2 divided doses for a mean duration of 85 ± 17 days. Ursodiol was continued until liver function normalized. Compared with previous therapy, ursodiol significantly reduced serum bilirubin and AST concentrations. Serum bilirubin and GGT concentrations were the earliest markers to decline at 1.5 ± 0.3 weeks and 1.6 ± 0.2 weeks, respectively. Decreased serum ALP, ALT, and GGT were not statistically significant.

One study evaluated the effects of ursodiol in 9 adults with short-bowel syndrome with PNAC, with remaining small

bowel length of 71 ± 18 cm (mean ± SEM, range 5–150), and who were PN-dependent for 13.9 ± 5.2 months.[11] Ursodiol 10–15 mg/kg/day (11.2 ± 0.8 mg/kg/day) was administered in 2 divided doses for one 2-month period (n = 9) or two 2-month periods (n = 5), each followed by a 2-month washout interval. Compared with nontreatment periods, the first and second ursodiol treatment periods were associated with significant reduction from baseline of serum GGT and ALT concentrations. Improvement in liver function did not correlate with remaining small bowel length. Decreased serum AST, ALP, and bilirubin concentrations were not statistically significant.

Summary

Ursodiol doses of 10–30 mg/kg/day in children and 10–15 mg/kg/day in adults improved the signs and symptoms of PNAC. However, the optimal timing and duration of ursodiol therapy in patients with PNAC remain unknown. Initiation of ursodiol therapy at the earliest increase in serum GGT or conjugated bilirubin concentrations may be necessary for best results. Although ursodiol therapy may improve liver function, its long-term effects on cholestasis and in preventing progression to end-stage liver disease are unknown. Because ursodiol efficacy is related to its intestinal absorption, recommended doses may not consistently achieve therapeutic effects in patients with short-bowel syndrome. Malabsorption is greatest in patients with absent terminal ileum or when combined with jejunal resection, and in the absence of ileocecal valve, which further exacerbates diarrhea.

The extemporaneously prepared ursodiol suspension in patients with short-bowel syndrome may be better absorbed than the capsule or tablet forms. Higher doses to overcome impaired absorption in patients with short-bowel syndrome may aggravate bile-induced diarrhea. Evidence from large, prospective, randomized, placebo-controlled, long-term follow-up studies is needed to assess the effects of ursodiol on the course and prognosis of PNAC.

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Ursodiol en Pacientes con Colestasis Asociada a Nutrición Parenteral

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Ann Pharmacother 2007;41:1867-72.

EXTRACTO

OBJETIVO: Revisar el papel del ácido ursodeoxicólico (UDCA, ursodiol) en el tratamiento de la colestasis asociada a nutrición parenteral (PNAC).

FUENTES DE INFORMACIÓN: Se llevó a cabo una búsqueda en la base de datos MEDLINE (1950–mayo 2007) con los siguientes términos de búsqueda: nutrición parenteral, colestasis, ácido ursodeoxicólico, y ursodiol.

SELECCIÓN DE FUENTES DE INFORMACIÓN Y MÉTODO DE EXTRACCIÓN DE INFORMACIÓN: Se incluyeron en esta revisión todos los artículos en inglés que evaluaban la seguridad y la eficacia de UDCA para el tratamiento de PNAC.

SÍNTESIS: Los beneficios de la administración de UDCA exógeno para el tratamiento de la colestasis pueden explicarse por su efecto de alteración sobre la composición y el flujo de la bilis y por su efecto citoprotector, estabilizador de la membrana y sus efectos inmunomoduladores. Dos estudios en animales, 2 informes de casos, y 6 estudios en humanos (2 estudios pediátricos prospectivos, y 3 retrospectivos, 1 estudio en adultos prospectivo) evaluaron la eficacia de UDCA en pacientes con PNAC. UDCA administrado a 10–30 mg/kg/día en niños y 10–15 mg/kg/día en adultos repartido en 2–3 dosis mejoró los signos bioquímicos y los síntomas clínicos de PNAC. Sin embargo, la leve mejora en los parámetros bioquímicos puede no resultar necesariamente predictiva de los resultados de los pacientes con PNAC. A las dosis recomendadas, UDCA puede no resultar efectiva en pacientes con síndrome del intestino corto (SIC) o con resección del íleo terminal debido a una reducción de la absorción de UDCA. Los estudios que apoyan la eficacia de UDCA en el tratamiento de PNAC están limitados por tamaños de población pequeños, ausencia de aleatorización y de grupo control, corta duración, y falta de contabilidad de las variables extrañas. Hasta el momento no se han realizado estudios de seguimiento a largo plazo, placebo-control, aleatorios, prospectivos y de larga duración que evalúen la eficacia, la dosis, y la duración óptima del tratamiento con UDCA para PNAC.

CONCLUSIONES: UDCA puede mejorar los signos bioquímicos y los síntomas clínicos de PNAC. Sin embargo, es necesaria la realización de estudios adicionales para la dosificación, el intervalo y la duración óptima de la terapia con UDCA, y sus efectos a largo plazo sobre el resultado de PNAC.

Traducido por Enrique Muñoz Soler

L'Emploi d'Ursodiol chez les Patients Souffrant de Cholestase Associée à l'Alimentation Parentérale

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Ann Pharmacother 2007;41:1867-72.

RÉSUMÉ

OBJECTIF: Revoir le rôle de l'acide ursodésoxycholique (AUDC, ursodiol) pour le traitement de la cholestase associée à l'alimentation parentérale (CAAP).

SOURCES DE DONNÉES: Une recherche MEDLINE (1950–mai 2007) a été effectuée en utilisant les mots clés alimentation parentérale, cholestase, acide ursodésoxycholique, et ursodiol.

SÉLECTION DES ÉTUDES ET EXTRACTION DES DONNÉES: Tous les articles de langue anglaise qui ont évalué l'efficacité et l'innocuité de l'AUDC pour le traitement de la CAAP ont été inclus dans cette revue.

SYNTHÈSE DE DONNÉES: Les avantages de l'administration exogène de l'AUDC dans le traitement de la cholestase peuvent être expliqués par les modifications qu'elle entraîne au niveau de la composition de la bile et du flux biliaire en plus de procurer des effets cytoprotecteurs, stabilisateurs de membrane, et immunomodulateurs. Deux études chez les animaux, 2 études de cas, et 6 études chez les humains (2 études prospectives et 3 rétrospectives en pédiatrie, 1 étude prospective chez les adultes) ont évalué l'efficacité de l'AUDC chez les patients avec une CAAP. L'AUDC à une dose de 10–30 mg/kg/jour chez les enfants et 10–15 mg/kg/jour chez les adultes en 2–3 doses fractionnées a amélioré les signes et symptômes biochimiques et cliniques de la CAAP. Cependant, des améliorations à court terme pour les paramètres biochimiques ne pourraient pas nécessairement prédire les résultats pour les patients atteints de CAAP. Aux doses recommandées, l'AUDC pourrait ne pas être efficace chez les patients atteint d'un syndrome de l'intestin court ou chez les patients qui ont subi une résection de l'iléon terminal en raison de l'absorption réduite de l'AUDC. Les études appuyant l'efficacité de l'AUDC dans le traitement de la CAAP sont limitées par les échantillons de petite taille, l'absence d'allocation aléatoire et de contrôles, leur courte durée, et le manque de discussion concernant les variables confondantes. Des études de suivi prospectives de plus grande envergure, à long terme, avec contrôle placebo évaluant l'efficacité, les doses optimales, et la durée de la thérapie à l'AUDC ne sont pas disponibles présentement.

CONCLUSIONS: L'AUDC pourrait améliorer les signes biochimiques et les symptômes cliniques de la CAAP. Cependant, les doses optimales de même que la durée de traitement et les résultats à long terme sur la CAAP ainsi que le pronostic requièrent d'autres études.

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