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COMPARATIVE EFFICACY OF URSODEOXYCHOLIC ACID AND DEXAMETHASONE IN REDUCING SEVERE PRURITUS IN PATIENTS WITH INTRAHEPATIC CHOLESTASIS OF PREGNANCY

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ABSTRACT

BACKGROUND: Intrahepatic cholestasis of pregnancy (ICP) is a hepatobiliary condition associated with impaired bile acid flow, which results in heavy maternal pruritus and an increased risk of adverse fetal outcomes such as preterm birth and stillbirth. Ursodeoxycholic acid (UDCA) is the first-line therapy, which reduces levels of bile acids and alleviating symptoms. In some cases a poor response to UDCA necessitates additional therapies. Dexamethasone, a corticosteroid, had been proposed as an alternative, however its use during pregnancy remains controversial and concerns exist regarding both its efficacy and safety. **OBJECTIVE:** To compare the efficacy and safety of ursodeoxycholic acid (UDCA) and dexamethasone in reducing severe pruritus in pregnant women diagnosed with intrahepatic cholestasis of pregnancy (ICP). **MATERIAL & METHODS:** This was a comparative, prospective study carried out in the Gynecology Department of Hayatabad Medical Complex, Peshawar, from June 2022 to May 2023. A total of 155 pregnant women with ICP whose diagnosis was based on clinical presentation of pruritus and elevated serum bile acid levels (>10 µmol/L) after the 20th week of gestation were included in this study. **RESULTS:** VAS pain scores decreased significantly in both groups over 4 weeks, however Group A (UDCA) diminished to a greater extent at all time points. At Week 1, the VAS score in Group A was lower than in Group B (6.2 ± 0.9 in group A vs. 7.1 ± 1.0 in group B). By Week 4, Group A mean VAS pain score decreased to 2.1 ± 0.6 and was significantly lower than Group B 3.9 ± 0.8. **CONCLUSION:** In patients with ICP, UDCA showed substantially superior efficacy compared to dexamethasone with respect to severe pruritus and serum bile acid levels. The UDCA group had better maternal and fetal outcomes, as well as a more favorable safety profile confirming its place as the first-line therapy for ICP management.

KEYWORDS: Ursodeoxycholic acid, dexamethasone, pruritus, bile acids, VAS, ICP.

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INTRODUCTION

Intrahepatic cholestasis of pregnancy (ICP) is a specific liver disease with impaired bile acid flow mainly in the second and third trimesters. This condition results in excessive biliary acids detected in maternal blood, clinically appearing as pruritus of pregnancy and elevated serum levels of bile acid. The most prominent symptom of ICP is severe itching, which can severely affect maternal quality of life and is linked to adverse fetal outcomes including preterm delivery, fetal distress, and stillbirths[1,2]

Ursodeoxycholic acid (UDCA) has gained broad acceptance as first-line therapy for ICP. It lowers serum bile acid levels, relieves itching and enhances liver function, resulting in better maternal and fetal outcomes[3,4] However, some patients with severe pruritus demonstrate inadequate response to UDCA only at baseline, putting into question the necessity for additional therapeutic options [5]. Dexamethasone, a type of corticosteroid, has been suggested as a possible adjunct or alternative therapy for the pruritus in ICP. Dexamethasone could provide symptom relief for patients with refractory itching by exerting anti-inflammatory effects and modulating bile acid metabolism[5]. However, the safety and teratogenicity of dexamethasone in pregnancy are still controversial [6,7].

Although the management strategies are increasingly emphasized, the underlying pathophysiology of itching in ICP is still complex and multifactorial. Elevated bile acids are believed to act as pruritogens through stimulation of sensory neurons present in the skin that induce the itch-scratch cycle[8]. In addition, hormonal changes in pregnancy (especially increased estrogen levels) may also contribute to cholestasis through impairment of bile acid excretion and increase of pruritic threshold[9,10]. This reinforces the need for more individualized therapy, not just directed at reducing pruritus, but also aimed toward correcting the underlying mechanisms of bile acid dysregulation.

Limited comparative studies exploring the efficacy and safety of UDCA compared to dexamethasone for severe itching during ICP are available. Research of this type is necessary to direct clinical decision making and tailoring management approaches in this difficult diagnosis.

MATERIAL AND METHODS

This was a comparative, prospective study carried out in the Gynecology Department of Hayatabad Medical Complex, Peshawar, from June 2022 to May 2023. Total 155 pregnant women with ICP whose diagnosis was based on clinical presentation of pruritus and elevated serum bile acid levels (>10 µmol/L) after the 20th week of gestation were included in this study.

Inclusion Criteria

- Pregnant women aged 18–40 years
- Gestational age ≥20 weeks
- Serum bile acid levels >10 µmol/L
- Severe pruritus defined as a Visual Analog Scale (VAS) score ≥7

Exclusion Criteria

- History of chronic liver disease or other liver pathologies

- Concurrent use of hepatotoxic drugs or other antipruritic treatments
- Multiple gestations
- Known fetal anomalies
- Contraindications to corticosteroid use (e.g., uncontrolled diabetes or infections)

Consecutive sampling was used to enroll 155 participants. Subjects were randomly assigned using a computer-generated randomization table into two groups.

Group A (n= 90): Patients in this group were treated with oral doses of UDCA at the dose of 15–20 mg/kg/day in divided doses.

Group B (n= 65): Patients in this group were treated with dexamethasone oral 8 mg/day for 7 days, then gradually reduced (if clinically indicated).

The primary outcome was the reduction in severity of pruritus measured by the Visual Analog Scale (VAS), from 0 (no itch) to 10 (worst itch imaginable). Secondary outcomes were serum bile acid levels and liver function tests (ALT, AST) before and after intervention, as well as maternal and fetal outcomes (e.g. preterm birth, fetal distress). Severity of pruritus was assessed at baseline and at 1 week, 2 weeks, and 4 weeks during treatment. Blood specimens were collected at the same intervals for measuring serum bile acid level and liver function tests. Data were analyzed using SPSS version 25.0. Statistical significance was defined as p-value ≤ 0.05.

RESULTS

Baseline characteristics of the two groups were comparable. Participants had a mean age of 28.4 ± 4.7 years in the UDCA group and 29.1 ± 5.1 years in the dexamethasone group (p = 0.348). The gestational age at diagnosis was similar in both groups (32.5 ± 2.8 weeks vs. 32.8 ± 2.5 weeks, p = 0.512). There was no statistically significant difference in baseline serum bile acid levels, ALT, AST, or pruritus VAS scores (p > 0.05). Table 1

Table-1: Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	Group A	Group B	p-value
Age (years)	28.4 ± 4.7	29.1 ± 5.1	0.348
Gestational age (weeks)	32.5 ± 2.8	32.8 ± 2.5	0.512
Serum bile acid (µmol/L)	45.6 ± 12.3	46.8 ± 13.5	0.614
ALT (U/L)	88.5 ± 20.1	91.2 ± 18.7	0.412
AST (U/L)	84.7 ± 19.4	87.9 ± 21.2	0.437
VAS score for pruritus	8.6 ± 0.8	8.7 ± 0.7	0.541

VAS pain scores decreased significantly in both groups over 4 weeks, however Group A (UDCA) diminished to a greater extent at all time points. At Week 1, the VAS score in Group A was lower than in Group B (6.2 ± 0.9 in group A vs. 7.1 ± 1.0 in group B). By Week 4, Group A mean VAS pain score decreased to 2.1 ± 0.6 and was significantly lower than Group B 3.9 ± 0.8. Table-2

Table-2: Primary Outcome: Reduction in Pruritus (VAS Score)

Time Point (VAS pain)	Group A	Group B	p-value
Baseline	8.6 ± 0.8	8.7 ± 0.7	0.541
Week 1	6.2 ± 0.9	7.1 ± 1.0	0.004

Time Point (VAS pain)	Group A	Group B	p-value
Week 2	4.3 ± 0.7	5.8 ± 0.9	0.030
Week 4	2.1 ± 0.6	3.9 ± 0.8	0.002

As elaborated in Table-3, Group A experienced a greater reduction in serum bile acid levels compared to Group B throughout the study. Similarly, ALT and AST levels showed more substantial declines in Group A.

Table-3: Secondary Outcomes

Time Point (Bile Acid (µmol/L))	Group A	Group B	p-value
Baseline	45.6 ± 12.3	46.8 ± 13.5	0.614
Week 1	32.5 ± 10.4	39.8 ± 12.7	<0.001
Week 2	20.1 ± 8.7	30.4 ± 10.9	<0.001
Week 4	12.3 ± 6.2	22.9 ± 8.5	<0.001

The incidence of preterm birth 9(10%) and fetal distress 12(18.5%) was lower in Group A as compare to Group B, though not statistically significant. No stillbirths were reported in either group. Transient hyperglycemia 5(8%) and gastrointestinal discomfort 4(6%) were observed more frequently in Group B as compare to Group A. Table-4

Table-4: Maternal and Fetal Outcomes & adverse events

Outcome	Group A	Group B	p-value
Preterm birth	10% (9/90)	18.5% (12/65)	0.134
Fetal distress	8% (7/90)	13.8% (9/65)	0.216
Adverse events			
Gastrointestinal discomfort	5% (5/90)	8% (5/65)	0.462
Transient hyperglycemia	0% (0/90)	6% (4/65)	0.029

DISCUSSION

This study assessed the effect of ursodeoxycholic acid (UDCA) and dexamethasone on the severity of pruritus in pregnant women with intrahepatic cholestasis of pregnancy (ICP). The results demonstrate that UDCA can significantly reduce pruritus, lowering the serum bile acid levels, and enhance liver function compared with dexamethasone, therefore, reaffirming its first-line status in ICP.

Pruritus, the prominent symptom of ICP, is related to the increased levels of bile acids in maternal circulation, which act as pruritogens for the sensory nerve cells within the skin. In this study, a significant reduction in pruritus severity was observed in the UDCA group compared to the dexamethasone group, as VAS pain scores decreased from 8.6 to 2.1 over a 4-week period in the UDCA group compared to 8.7 to 3.9 in the dexamethasone group. The findings support previous research showing that UDCA effectively reduces pruritus by improving hepatic clearance and bile acid level, which lowers serum bile acids and the itching they cause [11,12]

Dexamethasone had a more modest improvement in terms of pruritus relief. Dexamethasone, classified as a

corticosteroid, exerts downstream anti-inflammatory effects that may influence the pathway of pruritus yet lacks the biliary acid modulatory properties of UDCA[13,14] Our findings suggest that dexamethasone would still be helpful in refractory patients, but is not a viable replacement for UDCA in ICP pruritus cases as a single agent.

While both therapy groups experienced a drop in serum bile acid levels, the UDCA group (group A) experienced a more pronounced decline. Bile acid levels dropped by 73% in group A and 51% in group B at the end of the study. These findings align with earlier studies showing that UDCA enhances the excretion of bile acids and the protection of hepatocytes against bile acid-induced liver injury, leading to improved liver function and less bile acid accumulation[15, 16]

The degree of decrease in liver enzymes (ALT and AST) was also greater in the UDCA group. ALT levels dropped by 48% for patients on UDCA by week 4, versus 30% for patients on dexamethasone. Moreover, UDCA can reduce liver injury and ameliorate pruritus, corroborating the hepatoprotective characteristic [17].

Importantly there was no statistically significant association with preterm birth or fetal distress betxwn groups but the rate of preterm birth was lower in those receiving UDCA (10% vs. 18.5%) as well as the incidence of fetal distress (8% vs. 13.8%). These results imply that UDCA may help to mitigate the adverse fetal outcomes by achieving better control of bile acid levels. Higher bile acids are tied to a higher risk of preterm birth, fetal distress, and still birth by inducing placental vasoconstriction and impaired fetal oxygenation [18]. Therefore, the trends noted in this study may be due to UDCA's protective effect on the fetal-placental unit.

Compared to dexamethasone, UDCA had a much better safety profile. Gastrointestinal discomfort was reported in both groups, but transient hyperglycemia was found only in the group B (6%). This is consistent with known corticosteroid-related adverse events, especially regarding glucose metabolism [19]. The fact that there were no serious adverse events seen in either group affirms that both medications seem overall safe when used in the proper clinical context, although UDCA with its comparatively less aggressive side effect profile is more preferable to use on a long-term basis.

The study had some limitations, which needs to be highlighted: small sample size and single-center design. Furthermore, a short follow-up duration of four weeks may not be sufficient to assess long-term maternal and neonatal outcomes, especially those following delivery. Strengthening this, the study did not assess dexamethasone alone compared to UDCA alone, nor did it assess the additive or synergetic effect of UDCA along with dexamethasone, which should have been informative in understanding the effective therapy in cases of resistance.

CONCLUSION

In patients with ICP, ursodeoxycholic acid (UDCA) is more effective than dexamethasone at reducing severe pruritus, elevating serum bile acids, and enhancing liver function. Because UDCA had a higher safety profile, there were also fewer adverse events. Dexamethasone provided some alleviation, but the effects were less pronounced and the side effects were more common. With dexamethasone reserved for refractory ICP cases, these findings support UDCA as the first-line treatment for ICP. Future research should explore combination therapies and long-term maternal and fetal outcomes to optimize treatment strategies.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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AUTHORS' CONTRIBUTIONS:

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared

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