Addition of dextrose 3.5% to intrathecal sufentanil for labour analgesia reduces pruritus

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Purpose: To determine whether the addition of a low concentration (3.5%) of dextrose would minimize pruritus while maintaining the quality of analgesia.

Methods: In a double blind study 48 parturients in early labour were randomized to one of two study groups: dextrose (Dex, $n = 24$; 10 μg sufentanil in dextrose 3.5%), or normal saline (NS, $n = 24$; 10 μg sufentanil in normal saline). Parturients received the study drug as the intrathecal injection of the combined spinal-epidural (CSE) technique for labour analgesia. Duration and degree of analgesia were measured until epidural analgesia was initiated or delivery of the baby. The intensity and distribution (above T_6 , T_6 - L_1 , and below L_1) of pruritus were measured at five minute intervals during first 25 min after injection.

Results: Quality and duration of analgesia did not differ between groups, but the overall incidence of pruritus was less in the Dex group (88% vs 42%, $P = 0.001$). Within each region, the incidence of pruritus was less in the Dex group. In patients who had pruritus, for the Dex group, the incidence of pruritus in the upper region ($> T_6$) was lower than the NS group. There was no difference in the lower regions.

Conclusion: The addition of dextrose 3.5% to intrathecal sufentanil reduced the incidence of pruritus without affecting the duration or quality of analgesia in parturients in early labour. The distribution of pruritus in the Dex group was limited to below T_6 suggesting that pruritus to intrathecal sufentanil is mediated at the spinal level.

Objectif : Vérifier si l'ajout d'une faible concentration (3,5 %) de dextrose réduit le prurit pendant le maintien de l'analgésie.

Méthode : Lors d'une étude à double insu, 48 parturientes en début de travail obstétrical ont été réparties en deux groupes : dextrose (Dex, $n = 24$; 10 μg de sufentanil dans du dextrose à 3,5 %) et soluté physiologique (SP, $n = 24$; 10 μg de sufentanil dans un soluté physiologique). Elles ont reçu le médicament étudié en injection intrathécale comme composante d'une analgésie rachidienne et périurale combinée (RPC). La durée et le degré de l'analgésie ont été mesurés jusqu'à ce que l'analgésie périurale soit commencée ou jusqu'à la naissance du bébé. L'intensité et la distribution (au-dessus de T_6 , T_6 - L_1 , et sous L_1) du prurit ont été mesurées à cinq minutes d'intervalle pendant les 25 premières min après l'injection.

Résultats : La qualité et la durée de l'analgésie n'ont pas présenté de différence intergroupe, mais l'incidence globale de prurit a été plus faible dans le groupe Dex (88 % vs 42 %, $P = 0,001$). Pour chaque zone, l'incidence de prurit a été moindre dans le groupe Dex. L'incidence de prurit dans la zone supérieure ($> T_6$) a été plus faible chez les patientes du groupe Dex que chez celles du groupe SP. Le prurit de la zone inférieure ne présentait pas de différence intergroupe.

Conclusion : L'addition de dextrose à 3,5 % à du sufentanil intrathécal a réduit l'incidence de prurit sans changer la durée ou la qualité de l'analgésie chez des parturientes en début de travail. La distribution du prurit chez les patientes du groupe Dex s'est limitée à la zone sous T_6 , ce qui laisse croire à l'existence d'une médiation médullaire du prurit relié au sufentanil intrathécal.

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INTRATHECAL opioids have been used successfully in providing excellent analgesia for labour.^{1,2} In the last decade, the popularity of the combined spinal-epidural (CSE) technique has led to increased use of intrathecal sufentanil or fentanyl to provide analgesia for labour. Although CSE with sufentanil is associated with fast onset and excellent analgesia, the limited duration of action and the high incidence of pruritus have limited its wide acceptance as standard of care.

Drugs, including bupivacaine, have been added to intrathecal sufentanil to improve the duration of analgesia.³⁻⁵ Similarly, adding dextrose to make a hyperbaric solution has been attempted to control pruritus by limiting the spread of sufentanil.^{6,7} A spinal-level interaction producing pruritus is consistent with the onset and duration of pruritus.⁸ Because normal saline solution is slightly hypobaric, and because parturients usually stay in a head-up position following induction of regional analgesia for labour, the intrathecal injection of sufentanil in saline tends to spread cephalad.^{9,10}

The addition of dextrose 7.5% or 5% to sufentanil resulted in reduced spread of pruritus in previous studies,^{6,7} but it also reduced the duration of analgesia. We hypothesize that too much dextrose adversely affected the spread of sufentanil and that a lower concentration of dextrose would minimize pruritus but maintain the quality of analgesia. Thus, in a prospective, double-blind study, we examined the effect of a lower concentration (3.5%) of dextrose added to intrathecal sufentanil on the duration and quality of analgesia as well as the incidence, intensity, and distribution of pruritus.

Materials and methods

After receiving Institutional Review Board approval of the study protocol and informed consent from the participants, 48 parturients were enrolled in the study. The study size was estimated by power analysis, and the study population consisted of healthy parturients with singleton gestations in early labour (cervical dilation < 6 cm) requesting regional analgesia for labour and delivery. Patients with preeclampsia, diabetes, or other serious medical diseases were excluded.

The participants were assigned to one of two groups in a double-blind, randomized study: dextrose (Dex) or normal saline (NS). The study solutions were made by an anesthesiologist who was not the data-collector. For the Dex group, a solution of 10 µg sufentanil in dextrose 3.5% was made by taking 2 ml of the following 10 ml solution: 1 ml 50 µg·ml⁻¹ sufentanil, 3.5 ml dextrose 10%, and 5.5 ml normal saline. For the NS group, 10 µg sufentanil in normal saline was

made by taking 2 ml of the following 10 ml solution: 1 ml 50 µg·ml⁻¹ sufentanil, and 9 ml normal saline.

Each parturient received CSE labour analgesia. A fluid bolus of 500 ml lactated Ringer's solution was administered. With the patient in the sitting position, the L₂₋₃ or L₃₋₄ interspace was identified. The epidural space was identified with loss of resistance to air with a 9-cm, 18-ga Tuohy needle. A 12-cm, 27-ga Whitacre needle was then passed through the epidural needle into the subarachnoid space (both needles were manufactured by Becton Dickinson Company, Franklin Lakes, New Jersey). After seeing free-flowing cerebrospinal fluid, 2 ml of the study solution were injected and the spinal needle was removed. A 20-ga epidural catheter was then inserted 4 cm into the epidural space. The patient was positioned in a semi-recumbent position (head of the bed 20°–40°) and in left uterine displacement.

The parturients continued to labour and epidural analgesia was only administered if the patient requested additional pain medication. Duration of action for the study drug was defined as the time from intrathecal injection to request for epidural analgesia and was only calculated for those patients who requested epidural analgesia. If a patient delivered without requesting epidural analgesia, they delivered while the spinal sufentanil was still working, and duration of action could not be calculated.

Measurements of the degree of analgesia, and the intensity and spread of pruritus were taken at the time of injection, three minutes after injection, and every five minutes thereafter up to 25 min after injection. Additional measurements were noted when patients requested additional analgesic medications (if applicable) and when the baby was delivered. A visual analog score (VAS) of pain (0 = no pain, 10 = worst pain), and a pruritus score were recorded. The intensity of pruritus was measured on a 0 to 3 scale, where 0 = no itching, 1 = itching only when questioned, 2 = complaining of itching, and 3 = medication requested to relieve itching. Pruritus was considered clinically important if the maximum measured score was 2 or 3. Further, the distribution of pruritus was recorded for specific anatomic regions, including the chest, neck, or face (above T₆), abdomen or lower back and buttocks (T₆–L₁), and legs and perineum (below L₁).

Statistical analysis

A two-sample t test was used to compare continuous data (age, height, weight, cervical dilation, and duration of analgesia) with serial data (VAS for pain). The Fischer Exact test was used to compare the proportion data for the incidence of nulliparity with pruritus

between the two groups. The Fischer Exact test was also used to compare proportion data for the severity and distribution of pruritus between those patients who reported pruritus in each group. P -values < 0.05 were considered statistically significant.

Results

Forty-eight parturients (24 in each study group) were enrolled and received combined spinal epidural labour analgesia. There were no differences in age, height, weight, percentage nulliparous, or cervical dilation between the two groups (Table I).

Quality and duration of analgesia did not differ between the two groups (Table II). In both groups, all parturients had excellent analgesia with no difference in minimum VAS for pain between the groups. There was no difference in the number of patients who delivered under the study medication alone (NS, $n = 8$; Dex, $n = 10$). The duration of action did not differ between the groups.

The incidence of pruritus, defined as any score other than 0 (no itching), was 88% (21 of 24 parturients) in the NS group, and 42% (10 of 24) in the Dex group ($P = 0.001$) (Figure 1). In addition, within each anatomic region, the NS group had a higher incidence of pruritus.

TABLE I Demographics.

<i>Demographics</i>	<i>NS group (n=24) Mean</i>	<i>Dex group (n=24) Mean</i>	<i>P</i>
Age (yr)	23.5 $\pm$ 5.2	25.3 $\pm$ 6.3	0.21
Weight (kg)	82 $\pm$ 21.7	81 $\pm$ 16.1	0.79
Height (cm)	163 $\pm$ 4.7	162 $\pm$ 7.8	0.35
% Nulliparous*	58%	75%	0.22
Cervical Dilation	4.6 $\pm$ 1.2	4.3 $\pm$ 1.3	0.33

NS = Normal Saline; Dex = Dextrose. Mean $\pm$ SD.

* Percentages and P -value reported from Fischer's Exact test.

Because the overall incidence of pruritus was different, the incidence of clinically important pruritus and the distribution of pruritus were determined and compared only in the subgroup of patients who experienced pruritus rather than in the entire study population. The incidence of clinically important pruritus, defined as a score of 2 or 3, among patients who had pruritus was lower in the Dex group (NS, 19 of 21; Dex, 5 of 10; $P = 0.012$) (Figure 2).

In addition, there was a difference between the two groups in the distribution of pruritus (Figure 3). For the above T₆ region (chest, neck, face), the Dex group (2 of 10) showed less pruritus than the NS group (19 of 21) ($P = 0.005$). In contrast, there were no differences in the T₆-L₁ and below L₁ regions.

Discussion

Pruritus occurs in 80% to 95% of parturients who receive spinal sufentanil for labour analgesia.^{1,2} Limiting pruritus would help improve patient satisfaction with intrathecal sufentanil and the CSE technique used for labour analgesia. Because both analgesia and pruritus have a similar onset and duration, the interaction producing pruritus appears to be spinally mediated.⁸

When designing our study, we performed a pilot study with sufentanil in 5% and 7.5% dextrose, as well as in the lower concentration of dextrose (3.5%). Similar to previous studies, we found that the duration of analgesia appeared to be reduced in the more hyperbaric solutions (i.e., 5% and 7.5% dextrose). In contrast, we found that analgesia did not appear to be reduced in the 3.5% solution (unpublished data). Hence, we performed this prospective, randomized, double-blinded study.

In contrast to previous studies, which studied higher concentrations, we found that the duration of analgesia was not reduced in the hyperbaric 3.5% solution compared with the normal saline solution. Because

TABLE II Quality and duration of analgesia.

<i>Demographics</i>	<i>NS group (n=24) Mean $\pm$ SD</i>	<i>Dex group (n=24) Mean $\pm$ SD</i>	<i>P</i>
Minimum VAS	0.1 $\pm$ 0.3	0.2 $\pm$ 0.6	0.55
Maximum percent decrease VAS	98.6% $\pm$ 3.8	97.7% $\pm$ 6.6	0.58
Time to delivery with the addition of epidural analgesia	344 $\pm$ 116.0	315 $\pm$ 152.0	0.58
Time to delivery without the addition of epidural analgesia	110 $\pm$ 43.9	113 $\pm$ 35.7	0.87
Duration of action (min)	112 $\pm$ 29.5	131 $\pm$ 26.4	0.55
Percent delivered without epidural analgesia*	33.3% (n/a)	41.7% (n/a)	0.07

NS = normal saline; Dex = dextrose; VAS = visual analog scale.

* For percent delivered without epidural analgesia, no Mean or SD was reported, in which case the Fischer Exact test was performed to obtain a percentage and a P -value.

FIGURE 1 Number of patients with pruritus. The Dextrose (Dex) group ($n = 24$) had less pruritus than the normal saline (NS) group ($n = 24$) both overall and in each anatomical region ($P = 0.001$). Patients may have had pruritus in more than one anatomic region. above T₆ = chest, neck, or face; T₆-L₁ = abdomen and lower back; below L₁ = buttocks, legs, and perineum.

FIGURE 2 Incidence of clinically significant pruritus: comparison of incidence among patients who had any pruritus. When comparing the severity of pruritus among women in both groups who reported experiencing pruritus, patients in the Dextrose (Dex) group had significantly less incidence of severe pruritus than patients in the normal saline (NS) group ($P = 0.012$). Patients with clinically significant pruritus were defined as having a maximum pruritus score of 2 or 3.

the 3.5% solution was less hyperbaric than the 5% or 7.5% solution, sufentanil distribution was not expected to be as limited. This may account for the preservation of the analgesia duration.

On the other hand, similar to previous studies, the incidence and severity of pruritus was decreased. For severity, we chose not to use a VAS, but rather a clinically oriented, 0 to 3 scale. Since the major drawback

FIGURE 3 Distribution of pruritus: comparison of percentage among patients who had any pruritus. When comparing the distribution of pruritus among women in both groups who reported experiencing pruritus, patients in the Dextrose (Dex) group had significantly less incidence of pruritus in the above T₆ region than the patients in the normal saline (NS) group ($P = 0.05$). above T₆ = chest, neck, or face; T₆-L₁ = abdomen and lower back; below L₁ = buttocks, legs, and perineum.

of pruritus is patient dissatisfaction, the degree of pruritus causing this dissatisfaction was identified in patients by complaints or requests for medication (a score of 2 or 3). In addition, because we wanted to examine the overall incidence of pruritus as well as the incidence of clinically significant pruritus, we also included a score for pruritus where the patient did not complain (a score of 1). If no pruritus was present, a score of 0 was recorded.

The overall incidence of pruritus was markedly different between the two groups (Figure 1). In addition, when comparing the whole population, the differences at each region are significant (Figure 1). A more accurate comparison is to examine the distribution of pruritus in patients who had pruritus. When this was done, we still found a difference, but only in the upper region (Figure 3). Because there was no difference in the lower regions, the addition of dextrose only limited cephalad spread of pruritus. Similarly, pinprick levels were reduced in the Dex group within the upper region. The combination of these two observations provides further evidence that pruritus interaction occurs at a spinal level.

The severity of pruritus was also decreased. Similar to the study of distribution, the comparison was made only in the subgroup of patients who experienced pruritus. When a patient in the NS group had pruritus, the patient complained or requested medication almost all the time. Conversely, only half of the patients who experienced pruritus in the Dex group complained or requested medications.

Finally, since the use of ephedrine was not controlled or measured in this study, we cannot comment on whether the limited spread of intrathecal sufentanil reduced the incidence of hypotension. In addition, although no fetal heart rate changes were noted in the study, we did not specifically examine this issue. Both of these clinical questions should be examined in future studies.

In this population, creating a slightly hyperbaric solution for intrathecal sufentanil limited the incidence, severity, and spread of pruritus without affecting the analgesic properties of the sufentanil. By limiting pruritus, patient satisfaction may improve, and practitioner acceptance of the CSE technique for labour analgesia may increase. Further, the reduction in the distribution of pruritus and the similar reduction in the pinprick level of the hyperbaric group add further evidence that pruritus, from intrathecal opioids, is spinally mediated.

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