**A randomized controlled trail of a new treatment for labour dystocia**

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**Tweetable abstract:** Bicarbonate, a new way of treating labour dystocia

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**ABSTRACT**

**Objective:** Labour dystocia is an intransigent, high-profile issue in obstetric care, which causes significant maternal morbidity in low resource settings and maternal dissatisfaction and increased healthcare costs worldwide. Amniotic fluid lactate, (AFL), values have recently been shown to reflect the metabolic status of the uterus and high levels have a strong association with subsequent need for operative intervention due to dystocia. In sports medicine it is known that lactic acid can affect muscular performance but be decreased by bicarbonate given orally before physical activity. **Main Outcome Measures**: If an intake of bicarbonate, one hour before stimulation with oxytocin, changes the AFL levels and enhances delivery outcome in dystocic primiparous deliveries.

**Design:** Randomized controlled trial
**Setting:** Soder Hospital, Stockholm, Sweden.

**Population**: 200 dystocic primiparous deliveries with an arrested labour progress according to the partogram

**Methods**: At the confirmation of dystocia, AF (amniotic fluid) was sampled, and the AFL- level was analyzed blinded. Deliveries were randomized to an intake of bicarbonate or not (bicarbonate, n=100 or no bicarbonate n=100). In the ‘non-bicarbonate group’, stimulation with oxytocin was started immediately. In the ‘bicarbonate group’, oxytocin was given one hour after the intake. New sampling of AF was performed after one hour in both groups.

**Results**: bicarbonate improved maternal and fetal acid-base status and maternal AFL levels. The frequency of spontaneous vaginal delivery after treatment with bicarbonate was increased (67 vs 84 %, p=0.007), without affecting the fetal outcome.

**Conclusion**: A significant and clinically useful increased rate of spontaneous vaginal delivery resulted from bicarbonate ingestion by dystocic primiparous women. This was associated with decreased lactate in amniotic fluid and improved acid-base balance. This simple, low cost treatment, by reducing the need for operative delivery, has the potential to improve maternal morbidity and improve maternal satisfaction worldwide.

**Keywords: Dystocia, AFL, bicarbonate**

**Introduction**

Women and new-borns suffer high levels of morbidity as a result of a prolonged labour 1, 2. The ultimate reason why labour arrests is still unknown 3. When a dystocic delivery presents, oxytocin is recommended 4-6. An individualized treatment does not exist, and arrested labour is handled according to adopted clinical guidelines, rather than taking into account the status of the uterus. This in turns reflects the lack of understanding of the underlying causes of dystocia.

The uterus is one of the human body’s biggest muscles and it is composed mainly of muscle. For labour to end successfully, the uterus needs to produce strong, coordinated and effective contractions. Under exertion, lactic acid is produced by glycolysis in all human cells. Glycolysis mainly occurs under hypoxic conditions; but unusually, the uterus is highly glycolytic and produces lactate even under normoxic conditions 7. Repeated transient hypoxia is a normal feature of labour as the uterine vessels are occluded during each contraction 8-10. During a dystocic labour these periods will be extended, and the levels of pH and lactate in the tissue will decrease and increase respectively 11. Decreasing pH leads to intracellular acidification and an inhibition of the Ca2+ channels in the myometrial cells 12. A decreased inflow of Ca2+ into the muscle leads to weaker and consequently less effective contractions 13. New studies show a significant correlation between acidification of the uterine tissue, labour contractions and the effect of oxytocin 14.

Importantly, lactate produced by myometrial cells is mirrored by lactate in amniotic fluid 15. High levels of AFL are shown to be over-represented in dystocic deliveries compared to deliveries with a normal labour progress 16-18.

Athletes manage their expected lactic shock during exercise by drinking baking soda dissolved in water (bicarbonate 0.3g / kg body weight) about one hour before their physical activity19,20. An intake of bicarbonate will neutralize the lactic acid formed during exertion. For athletes this ingestion of bicarbonate has been associated with improvements performance and coping a little bit better when great physical effort is required 21-24.To the best of our knowledge such a strategy has not been tested for women in labour.

The aims of this study were to determine if an oral intake of bicarbonate in women with labour arrest could change the level of AFL and increase the frequency of spontaneous vaginal deliveries among dystocic primipara’s deliveries.

**METHODS**

A randomized controlled trail of 200 primiparous women in active labour was performed at South Hospital, Stockholm, Sweden during 2013-2014. The study was approved by the regional ethics committee at the Karolinska Institute, Stockholm, Sweden (file record: 2012/1275-31/3).

In all deliveries at the clinic, a partogram was recorded according to clinical routines. If cervical dilation crossed the action line in the partogram or if labour progress was arrested for two hours or more the delivery was considered to be dystocic. Oxytocin was then suggested for stimulation as per hospital protocol.

*Inclusion criteria* for the study were: primiparity, singleton pregnancy, with an arrested labour progress according to the partogram with a need for oxytocin. Gestational age was between 37-42 weeks, and no maternal /fetal chronic and/or pregnancy-related conditions. *Excluded* were multiparous women, deliveries with non-cephalic presentation, multiples, deliveries with fetal chronic and/or pregnancy-related conditions, IUFD (Intra Uterine Fetal Death) or premature < 37 weeks of gestation. A flowchart of the study design is presented in figure 1.

200 consecutive deliveries were considered to be dystocic according to the definition, they fulfilled inclusion criteria’s for the study, and the woman was asked, by the midwife in charge, for her consent to study inclusion.

In all included deliveries a sample of AF was collected vaginally at the time of inclusion, and the AFL-value was analyzed immediately at the bedside by a research midwife. The AF samples were analyzed blinded, and the results were stored in the device, and not shown until after delivery. The device (LMU061, ObsteCare AB, Sweden) was adapted for measurement of lactate in amniotic fluid, and measured lactate concentration in AF with a coefficient of variation of approximately 3 % at a lactate concentration of 11mmol/l. The lactate recognition system was based on lactate oxidase with amperometric detection of the enzymatically produced hydrogen peroxide.The device requires only 0.5 ml of amniotic fluid 17, 18, 25.

In earlier publications the influence of meconium and blood in AF has been studied 17. Meconium did not appear to affect the analysis of AFL, but a high concentration of blood (>10 %) decreases the values. Amniotic fluid samples with meconium were therefore included, but AF tinged with a visible high degree of blood has been removed from the analysis in this study.

In all included deliveries a maternal venous blood sample for analyze of the maternal acid-base status was collected at the time of inclusion. The ABL 800 analyser (Bayer®) available in the delivery ward was used

A sealed envelope was drawn at inclusion and a randomization into two groups was performed. One group was treated with two bags of Samarin® (=bicarbonate group). Each package of ‘Samarin original’ has an active substance of sodium bicarbonate 2.13g and tartaric acid, citric acid, sodium, potassium and silica. Two bags of Samarin® was mixed in a glass of water (200ml) and ingested during a couple of minutes by the labouring woman one hour before stimulation with oxytocin started. The other group (=non-bicarbonate group) received no Samarin® and started oxytocin immediately, according to local clinical guidelines (figure1). After one hour, another sample of AFL and blood was collected from all 200 women, and the Samarin® group then commenced stimulation with oxytocin if still no progress of labour was identified (figure1).

The Apgar score at 1 and 5 minutes after delivery was determined by the midwife in charge. An arterial cord blood sample was drawn from a double-clamped segment of the cord before the new-borns first cry, and analysed within a few minutes. Maternal and fetal data was collected from medical files after delivery and analysed according to group.

**Statistics**

A power calculation was made. To estimate the difference (with 83% power) in AFL-levels with a precision of approximately 10 percentage in the groups with or without bicarbonate, at least 160 women (80 with bicarbonate and 80 without) needed to be recruited to make the result statistically significant. We based our calculation on Sample Power 3.0.

Statistical analyses were performed using SPSS 22.0 (SPSS Inc. Chicago, Illinois, USA), and the statistical Package Statistica for Windows, version 13.0 (Stat Soft, Tulsa, Oklahoma, USA). Differences between the groups (with/without Samarin®) were tested by t-test for parametric variables (SD) and chi-squared test for categorical variables (%) in expected frequencies < 5, Fisher´s exact test was used. Logistic regression was used to study the association between spontaneous vaginal delivery and each of the independent factors: maternal age, maternal height, gestational age, fetal weight, fetal height, head circumference, gender of the fetus and the use of Samarin®. Our model strategy was as follows: first, unadjusted associations with each factor were studied; second, the adjusted association with respect to the risk factors measured was studied in a multivariable model with all factors included. Finally, to study whether the rate of spontaneous vaginal delivery differed in any subgroup with respect to the intake of Samarin®, we added an interaction term between Samarin® and each of the other factors to the adjusted model (sequentially). P-values below p < 0.05 were regarded as statistically significant.

**RESULTS**

In this RCT-study 200 primiparous women in labour were included. 11 deliveries were excluded after inclusion as sampling of amniotic fluid was missing or amniotic fluid was tinged with a high degree of blood (fig.1 flow chart).

Maternal background data did not differ between the two groups when age, smoking habits and BMI were compared. New-borns in the non Samarin® group were bigger, older and more males were born compared with the group where Samarin® had been ingested (table 1).

Among included deliveries, 84 vs. 67 % (Samarin® vs. nonSamarin®) had a spontaneous vaginal delivery rate (p= 0.007, table 2), and 6.7 vs 24.2 % (Samarin® vs. nonSamarin®) were delivered by vacuum (p=0.007, table 2).

New-borns were generally healthier at delivery in the group of Samarin®, they had a significant higher pH (p<0.01) and lower BE in cord blood at delivery (p=< 0.01, table 2). No neonate in the Samarin® group had an apgar score < 7, 5’minutes compared to 2 newborns in the nonSamarin® group.

An intake of Samarin®, one hour before augumentation with Oxytocin, affected the woman acid-base status in blood and her AFL levels in a positive way. A significant increase of maternal pH (p < 0.001) and decrease of Pco2 (p= 0.04) was shown. Also AFL levels were decreased with a mean value of -0.7 mmol/l, from 8.6 to 7.9 mmol/l (p=0.05). Among deliveries where the AFL level was high (>10.1mmol/l) at the first sampling, the decrease of AFL was most notable, from 10.9 to 9.9 mmol/l in mean (p < 0.001, table3a).

In the group where no Samarin® had been ingested, no differences were seen in maternal acid-base status, nor in AFL levels. In the nonSamarin® group with high levels of AFL (>10.1 mmol/l) at first sampling, and in marked contrast to the bicarbonate ingesting group, the value of AFL significantly increased from 10.7 to 11.9 mmol/l after 1 hour of stimulation with oxytocin (p < 0.001, table 3b).

Fetal head circumference < 35cm and an intake of Samarin® before augumentation with oxytocin were all associated with an increased likelihood of spontaneous vaginal delivery in included deliveries (table 4).

No significant association was found between maternal age, maternal height, fetal height and gender. No significant interactions between intake of Samarin®, and each of the other factors were detected (p > 0.48 for all tests of interactions). This implies that the sensitivity for spontaneous vaginal delivery among women in dystocic deliveries who had been drinking Samarin® before augumentation was 2.3 times higher compared to women without an intake of Samarin®, irrespective of the levels of the other factors (table 4).

 **DISCUSSION**

**Main Findings**

In this RCT study of 200 primiparous women with confirmed labour dystocia according to the partogram, half had bicarbonate (Samarin®) as a drink. Samarin® was given to help the uterus recover from the muscular changes associated with labour dystocia 11. Samarin® is a Swedish product used by many pregnant women when they have indigestion problems. The product is palatable, and sold in small paper packages in grocery stores. It is considered to be “food” and not pharmaceutical. Two pieces of Samarin® contains 4.26g of bicarbonate. In the 100 include deliveries where Samarin® was ingested one hour before augumentation with oxytocin was started, Samarin® affected the woman acid-base status and her AFL levels significantly in a positive way. In the deliveries where the AFL level was high from the beginning the decrease was most notable. In the control group no differences were seen in maternal acid-base status, or AFL levels, which continued to rise. What is notable is that even fetal outcome was improved in the bicarbonate group. New-borns were generally healthier ad had a significant higher pH and lower BE in cord blood at delivery. The explanation for this is probably that the environment in the uterus was improved during labour when bicarbonate had been given. Based on our understanding of uterine physiology, by correcting the local lactic acidosis which is associated with dystocia, vascular flow and thence uterine environment are improved. The improved flow and contraction pattern will be expected to benefit placental perfusion and fetal wellbeing. Previous studies from our research group shows that 75% of children who are affected at birth with a low pH in cord blood and a low Apgar score, also have high level of AFL at delivery 16. One can conclude that the use of bicarbonate during labour probably gives advantage not only for the labouring woman but also for her unborn child during a dystocic delivery, but this remains to be specifically investigated.

**Strengths and Limitations**

The strength of this study is that it is randomized, even if the size of the study is quite small. The proposed management of the arrested labours in the study has not been selected. A randomization has occurred and given directives for the treatment or no treatment. Some limitations of this study should be mentioned. Soder Hospital is a large city hospital in Stockholm and the women included in the study were older than the national average in Sweden, which might influence our findings. A third limb to the study could have been 100 women labouring well and for AFL and bloods to have been taken from them at corresponding time points to the non-Samarin® group. However studies where AF has been collected from normal deliveries have already been performed and reported several times 16-18, 25, and would have added no new data. Methodological strengths of the study are that AFL can be measured easily, quickly and routinely at the bedside, and if necessary a measurement provided in 15 seconds. Samarin® is ingested and palatable, well tolerated, does not require refrigeration and is relatively cheap. These features suggest this approach could be transferred to a low resource setting, where the effects of dystocia have far more serious effects on maternal and fetal outcomes of labours.

It is important to note that in the study of lactate and pH in dysfunctional labour 11, the changes were local (myometrial) not systemic, whereas the application of bicarbonate as Samarin® as in our study will produce systemic changes. It is however difficult to see how local i.e. myometrial applications of bicarbonate could be made non-invasively, and in any case, as large fraction of cardiac output will be delivered to the labouring uterus, systemic application can be considered appropriate.

**Interpretation**

Athletes use many different strategies to enhance their performance, including different accessories, diets, and ergogenic aids. Among the more popular ergogenic aids is the use of bicarbonate also referred to as “buffers”. The bicarbonate potentially provides the body with added resistance against fatigue caused by changes in acid-base balance. The popularity of “buffering” has generated research dating back to the 1930s, which continues to date 23.

In obstetric care no similar tradition is present. Muscular exhaustion is usually defined as a failure to maintain a required power output. The reason for uterine exhaustion during labour, known as dystocia, is probably multifaceted and includes both physiological and psychological components. What is clear, however, is that potential contributors to the uterine muscular fatigue during a dystocic delivery are metabolites associated with the anaerobic situation in the uterine muscle 11, 17, 18, 25.

A search of the literature finds no previous study administering bicarbonate to labouring women. Earlier studies, based around the idea that the work of labour will lead to dehydration, and that if labouring women are not adequately hydrated they may suffer acid-base balance disturbances, have been conducted. As reviewed by Dawood et al 26 there is evidence that if women are not freely drinking fluids, then additional iv fluids can decrease the length of labour. The number of Caesarean sections was also reduced. These data, although limited, are consistent with our data in that they support the hypothesis that the uterine environment changes during labour and correction of the metabolic consequences of uterine contractile activity will benefit mother and fetus. Specifically the findings of myometrial lactic acidosis in capillary blood from women labouring dysfunctionally 11 and tested here by administration of bicarbonate are supported.

The question arises, if ingested bicarbonate only initially improves the outcome of a dystocic delivery or if it has a longer acting effect. Would it therefore be useful in prolonged labours? Studies by Price, Moss, and Rance from 2003 27 showed that after ingested bicarbonate among athletics, improvements was identified not only initially but also in performances that occurred after the initial ingestion. The improvement was consistent with the long time period over which blood pH changes took place and were maintained. Their conclusion was that ingestion of bicarbonate can improve performance during prolonged intermittent types of exercise, when pH is decreasing and over greater exercise duration than had previously been considered. Childbirth can also be described as prolonged and intermittent in its effort, and thus bicarbonate may be expected to have a long lasting effect during labour. Further studies should be performed, where a more long-term effect during labour will be studied, and a repeated intake of Samarin® could be tested if needed. A question is also which doses that should be used. In this study much lower doses of bicarbonate than recommended among athletes, has been used. Further studies are needed to show which doses might be the most efficacious and if AFL levels could be used to guide individual doses. Another relevant question is, if a longer interval between bicarbonate ingestion and oxytocin administration was used, would it reveal increased contractility sufficient for labour to progress without the need for oxytocin, as the uterus recovers from the muscular metabolic effects.

A possible disadvantage of giving woman Samarin® to drink is that it can contribute to GI upset and thus some women may not tolerate it well. In this study no one in the bicarbonate group complained of GI upset.

 **Conclusion**

The level of AFL decreases among dystocic women who received Samarin®. The frequency of spontaneous vaginal delivery after treatment with Samarin® was increased, and even if we did not power the study to investigate neonatal outcomes, nevertheless we found better fetal outcome in the group with a maternal intake of Samarin®. Our question is if bicarbonate, at the right dose and frequency, could be an even better alternative and not only a complement to oxytocin in dystocic deliveries.

**What is already known on this topic**

* Labour dystocia is an intransigent, high-profile issue in obstetric care
* Labour dystocia causes significant maternal morbidity, mortality and dissatisfaction
* An individualized treatment of dystocic deliveries doesn’t exist

**What this study adds**

* Bicarbonate referred to as “buffers”, potentially provides the body with added resistance against fatigue caused by changes in acid-base balance
* Bicarbonate as a drink during delivery may help the uterus recover from the muscular changes associated with labour dystocia
* Bicarbonate given as a drink during delivery will increase the frequency of spontaneous vaginal delivery among dystocic deliveries

**Disclosure of Interests**:

EWI received in early 2000 a smaller number of shares in a company (ObsteCare AB, Sweden) that may use the results of the study commercially in the future. Over the past ten years, none of the authors received any shares, equity, promise of employment, or a named position on a company board. None of the authors has been asked by any organisation to write, be named in, or to submit the paper.

**Contribution to Authorship:**

EWI, SW and HÅ discussed the work and designed it. EWI collected the data and made the data analysis. All authors interpreted the results and wrote the report.

**Details of Ethics Approval**

The study was approved by the regional ethics committee at Karolinska Institutet, Stockholm (2012/1275-31/3). Written informed consent was obtained from all the women before inclusion in the study.

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