Oxytocin is Unequally Distributed in a Bag of Normal Saline â True or False?

Abstract:

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Abstract

Oxytocin infusion used in labour can sometimes be left hung on the stand for many hours. There has been no study to determine if oxytocin is equally distributed throughout the infusion bag and if the distribution stays the same with time. We postulated that there may be settling of the molecules such that oxytocin concentrates at the bottom of the infusion bag. Eight infusion bags were prepared by mixing 10 IU of oxytocin in 1 litre of normal saline. The infusion bags were hung on infusion stands for 8 hours after which 10 samples of 100 mls of the solution from each bag were taken in different containers and the concentration of oxytocin calculated using oxytocin specific Enzyme Immunoassay (EIA) in the different samples. No statistically significant correlation between the oxytocin concentration and the sample number was observed (p-value = 0.738). There was no obvious relationship between oxytocin concentration and the sample number in each bag. There was no evidence to suggest that a linear oxytocin concentration gradient develops in a bag of normal saline over an 8-hour period. In fact the distribution appears to be random and unequal.

Introduction

Oxytocin is a hormone produced by the posterior pituitary gland. It has a number of peripheral actions mediated by specific oxytocin receptors. The peripheral actions of oxytocin include uterine contractions during labour, excretion of milk during breast- feeding, role in sexual arousal, wound healing and behavioural control.[1] The uterine contracting properties of oxytocin were discovered by British pharmacologist Sir Henry Hallett Dale in 1906.[2] The milk ejection property of oxytocin was described by Ott and Scott in 1910[3] and by Schafer and Mackenzie in 1911.[4] In 1953, the chemical structure of oxytocin was elucidated almost simultaneously by DuVigneaud and associates in the United States and Tuppy in Austria. In the following year, DuVigneaud was able to synthesize oxytocin and, in 1955, Boissonnas evolved a method of manufacturing synthetic oxytocin on a commercial scale.[5] In regards to parturition, synthetic oxytocin is used for induction and acceleration of labour, delivery of the placenta and management of postpartum haemorrhage. The three ways of administering the drug are intravenous injection, intramuscularly and as an intravenous infusion.[6] Oxytocin has been given as an intravenous infusion for induction and, in cases of labour dystocia, to accelerate labour.

Labour dystocia is characterized by slow, abnormal progression of labour. It is diagnosed based on delays in cervical dilatation. Approximately one fifth of human labours have dystocia.[7] In the majority of cases of labour dystocia, there would be a response to oxytocin infusion as indicated by an increase in uterine contraction and change in cervical dilatation. However in some cases, even though there is an initial response to the infusion, the cervix fails to dilate fully and delivery by cesarean section is required. Explanations the above scenario, include problem with the passage (cephalopelvic disproportion), passenger (abnormal fetal lie or presentation) and power (inefficient uterine contraction and possibility of lactic acid accumulation which tires the uterine muscle and therefore lessens the efficiency and strength of muscle activity).[8,9] Our theory was based on a more simplistic assumption.

In the National Maternity Hospital, intravenous infusion of oxytocin is prepared by mixing 10 IU of syntocinon to 1L of 0.9% saline. A giving set is connected to the bag which is then hung on a stand. The infusion is started at a rate of 30 mls/hour with increments of 30 mls/hr every 15 minutes to a maximum of 180mls/hour aiming for a maximum of 7 contractions in 10 minutes for primips and 5 for multips. Sometimes, oxytocin infusion has to be stopped due to abnormal CTG or overcontraction leaving the infusion bag hung on the stand for many hours. There has been no study to prove that the concentration of oxytocin is equally distributed throughout the infusion bag and if its distribution stays the same with time. We postulated that with time, there may be settling of the molecules such that most of the oxytocin concentrates at the bottom of the infusion bag. This would mean that most of the oxytocin would be infused within the first few hours. This may explain why in some cases, there is an initial response to oxytocin where the cervix changes in consistency/ dilatation but fails to dilate fully despite hours of oxytocin infusion. Our aim was to test this theory.

Methods

Eight infusion bags were prepared by mixing 10 IU of Syntocinon in 1 litre of 0.9% saline. Giving sets were connected to each infusion bag and the solution run to the tip of the giving set. The bags were labeled A â H. The infusion bags were then hung on infusion stands, which were placed in a quiet room to prevent disturbance of the bags. They were left at room temperature for 8 hours. After 8 hours, 10 samples of 100mls of the solution from infusion bag A were taken in 10 different containers by opening the tap of the giving set. They were labeled A1- A10. This was repeated with the other infusion bags and the containers were labeled B1- B10 up to H1- H10. The concentration of oxytocin was then calculated using oxytocin specific Enzyme Immunoassay (EIA) in the different samples. The EIA kit uses polyclonal antibody to oxytocin to bind, in a competitive manner, the oxytocin in the sample. Following reagent preparation and assay procedure as per the protocol supplied with the kit, the enzyme reaction produces a yellow colour, which is read on a microplate reader at 405nm. The intensity of the bound yellow colour is inversely proportional to the concentration of oxytocin in the sample. The measured optical density is used to calculate the concentration of oxytocin. We tested 8 infusion bags as it provided enough total samples to fill all the plates on the EIA kit. We collected the samples after 8 hours as it is a realistic length of time for labouring women to be on oxytocin.

Results

Casual inspection of the raw results failed to show any discernible pattern. The distribution of oxytocin concentration in each bag A-H is shown in Figure 1. It shows a widely varying oxytocin concentration from each sample in each bag without any obvious pattern. One would expect the distribution to be a straight line (homogenous distribution line in Figure 1) across at 17ng/ml. This is based on the fact that 12.5 IU of oxytocin is equivalent to 21.4 mcg[10], and when 10 IU of oxytocin is mixed to 1L of 0.9% saline, it would give a concentration of 0.017mcg/ml (17ng/ml) which should have been detected in all sample had there been an equal distribution throughout the bag. When the oxytocin concentration is plotted against the sample number (1-10) for all infusion bag (Figure 2), there is still no obvious correlation between the sample number and the oxytocin concentration. The data was formally analysed with R version 2.11.1. Pearson product-moment correlation coefficient between oxytocin concentration and sample number was 0.34 (p-value = 0.74). This indicates a statistically insignificant positive correlation between oxytocin concentration and sample number.

Discussion

Labour dystocia is a common indication for delivery by cesarean section. There is continuing research into the causes and treatment of labour dystocia. In majority of cases, labour dystocia is corrected with oxytocin infusion. Our theory that oxytocin may settle at the bottom of an infusion bag was an important possibility to confirm or refute. However, the results of our experiment do not support our hypothesis that oxytocin settles to the bottom of a bag when left hanging for prolonged periods of time. The data actually displays a very weak, statistically insignificant increase in oxytocin in later samples. More importantly, our experiment shows a widely fluctuating concentrations of

oxytocin between the samples in each bag. This is an interesting and possibly clinically relevant observation. It could explain why some labour responds immediately to oxytocin infusion, while others require few hours of oxytocin infusion before changes in cervical dilatation is noted. The erratic concentration measured may indicate that the distribution of oxytocin in a bag of normal saline is actually random and unequal. However, these results should be interpreted carefully as one would expect a constant or smoother gradation in oxytocin concentration. Further research needs to be conducted with careful attention paid to assay accuracy and reproducibility to definitively answer whether oxytocin concentration varies in a bag of saline allowed to settle for a prolonged period of time.

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