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A COMPARATIVE STUDY OF TWO DIFFERENT HYDROXYETHYL STARCH IN GYNAECOLOGICAL SURGICAL PATIENTS

Gynecology

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ABSTRACT

Background: Hydroxy Ethyl Starch (HES) are mostly used perioperatively to protect intravascular compartment and replace losses. We planned this study to evaluate the effect of two different Hydroxy Ethyl Starch on the blood glucose & serum electrolytes in non-diabetic patient posted for gynaecological surgery under spinal anesthesia.

Material and method: in a prospective, randomized, controlled trial, 60 female patients , 18–70 years of age were included and randomly divided into 2 groups of 30 patients in each to receive either 6% HES 200 (pentastarch)-PS or 6% HES 130 (tetrastarch)-TS.

Results: Mean rise in BSL after 12 hours was 23.53±17.01 mg % & 26.20± 15.05 mg% in group PS & TS respectively. Mean change in serum sodium and chloride level ranged from -2.17±6.20 to 1.05±6.27 and -2.10±3.48 to -0.23±5.20 mEq/L respectively. There was a continuous decline in mean serum potassium level by 1.01, 1.26 mEq/L and and calcium level by 0.43, 0.34 mg% in group PS & TS respectively.

Conclusion: Both the groups produces a rise in Blood glucose level to a variable degree. There is no appreciable effect on serum sodium and chloride level while there is a marked drop in serum calcium and potassium which was evident even up to 12 hours. 6% HES 130 produces the less disturbances in serum calcium and serum potassium level so preferred in gynaecological surgeries.

KEYWORDS

Hydroxy Ethyl Starch (HES), Pentastarch, Tetrastarch, (RL), Blood Sugar Level (BSL), Serum Electrolyte Level, Gynaecological surgery

INTRODUCTION

Perioperative period is the period of hemodynamic vulnerability as well as metabolic dearrangements. Intravenous fluids used during this period is a mattern of concern. Liberal or fixed volume therapy, goal directed therapy (GDT) and restrictive (zero balance) fluid therapy has been advocated in literture regarding perioperative fluid administration. Restrictive (zero balance) fluid therapy is the currently used approach to manage fluid balance. As per this approach intraoperative loss is compensated with Crystalloid in 1.5:1 and colloids in 1:1 ratio.

Colloids might be useful for this approach. A colloid is used to restrict fluid volume and compensate blood loss in 1:1 ratio. It is a solution containing molecules that are large enough to be impeded by endothelial linings. They exert a pressure; "the colloid osmotic pressure" by virtue of the number of large molecules on one side of the barrier that cannot move. This oncotic pressure holds or draws water to it. Colloids vary in size from 20,000 to 450,000 Dalton. Size, shape and charge influence the ability of those molecules to move out of the intravascular space and larger the molecule, less likely it is to move out.

Colloids are starch or gelatin products and their base or carrier solution is usually normal saline. Hydroxyethyl starch is frequently used colloid. Hydroxyethyl starch was introduced in 1957 and the first generation Hetastarch introduced into clinical practice during the 1970s. HES is semisynthetic colloid produced by hydroxyethyl substitution of amylopectin, a D-glucose polymer obtained from sorghum or maize. So this conformationally different polysaccharide is difficult to metabolized by serum amylases. This leads to increase in half life of the HES and is more prominent when the hydroxyethyl residue bound to C2 or C6 position of glucose. Various molecular modifications during the 1980s and 1990s leave us with the second generation Pentastarches and subsequently third generation low molecular weight tetra starches in common use today. These above modification mainly done to increase in half life along with to decrease incidences of adverse effect.

Gynaecological surgical patients are mostly anemic due to chronic blood losses and are optimized preoperatively. Hydroxyethyl starch is commonly used fluid in these patients to restrict total fluid volume infused perioperatively. As these are starch derivatives and their base solution is normal saline so there is chances of hyperglycemia and electrolyte imbalance.

There are various studies regarding HES and their effect on hemodynamics, blood sugar level, coagulation defect. But the studies evaluating different HES with blood glucose level and serum electrolytes are limited. Taking into consideration the ill effects of hyperglycemia & electrolyte imbalance in the perioperative period & the frequent use of HES as volume expander, the present study was aimed to examine the effects of 6% HES- 200/0.5 (Pentastarch) and 6% HES- 130/0.4 (Tetrastarch) on the blood glucose & serum electrolyte (mainly Na+, K+, Cl- &Ca++) levels in non-diabetic patients undergoing gyenecological and perineal surgical procedures under spinal anesthesia.

MATERIAL AND METHODS

Study design: The study was designed as a prospective, open, controlled, and randomized trial. After approval from the institutional ethical committee, the study was conducted in the tertiary care hospital on 60 female patients of 18-70 yrs age who underwent gynecological surgery under spinal anaesthesia.

Groups: patients were divided into 2 groups of 30 each.
Group PS - 6% HES-200/0.5 (Pentastarch) - 15 ml/kg
Group TS - 6%HES -130/0.4 (Tetrastarch) - 15ml/kg

Exclusion Criteria of the study were patients with Diabetes Mellitus, renal disease or any other biochemical derangement due to the disease, patients on drugs that cause hyperglycemia (acetaminophen, steroids), patients on drugs that cause hypoglycemia (Octreotide), patients with low hematocrit value, patient refusal, patients who had a recent exposure to HES or allergy to HES.

Protocols to be followed

After thorough clinical examination, routine investigations for biochemical indices including fasting & postprandial (2hrs) blood sugar, serum electrolyte, serum calcium level etc. X-Ray chest, ECG & other special investigation if necessary.

After overnight fasting confirmed and informed written consent was taken, the patient was taken into the OT and allocated to groups according to how they were received in OT i.e. 1st patient allocated to group 1, 2nd patient to group 2 and so on.

An intravenous access was achieved with an 18G IV Cannula & a sample of blood was drawn & sent for blood sugar and serum electrolytes levels (Na+, K+, Cl- &Ca++). This reading was considered as basal or zero reading. Baseline parameters i.e. pulse, BP etc. were recorded and assigned HES (Pentastarch or Tetrastarch) was given at calculated dose (15 ml/kg). The spinal anaesthesia was given with inj. 0.5% Bupivacaine 3ml (Heavy). Patient was given oxygen @ 4L/minute through ventimask. All vitals have been recorded

throughout the surgery. After giving assigned HES the patients received Ringer Lactate as subsequent IV fluids till the final blood sugar reading is taken at the end of twelve hours from the basal reading. Blood sample for sugar and electrolyte level was taken after 60 minutes followed by two hourly (i.e.1, 3, 5, 7 and twelve hours) for next twelve hours. Urine output & any side effect were also recorded.
Statistical analysis: Data within the group was analysed using the paired t-test and between the groups was analysed using student t-test.

RESULTS:

Demographic profile in regard to age and weight is comparable between groups. Maximum numbers of patients were between 36-50 years age group. Most of the patients were between 46-60 kg weight groups.

BLOOD SUGAR LEVEL

Table 1 Mean blood sugar level (± S.D.) at various time intervals and Mean change in blood sugar level (± S.D.) in mg% from the baseline (0hrs)

Observation time(hrs)	Group-PS (6%HES200/0.5)			Group-TS (6%HES130/0.4)		
	Mean± S.D.	Mean change ± S.D. (% variation)	P value (sig.)	Mean± S.D.	Mean change ± S.D. (% variation)	P value (sig.)
0 (Basal)	95.83±12.22 [77-124]			94.17±11.11 [77-120]		
1	95.10±11.39 [77-126]	-0.73±11.50 [-0.77%]	0.7294	94.90±12.02 [70-117]	0.73±11.99 [0.78%]	0.7399
3	97.40±13.20 [75-134]	1.57±14.50 [1.63%]	0.5585	101.97±14.05 [85-139]	7.80±12.95 [8.28%]	0.0026
5	106.73±17.53 [80-154]	10.90±18.12 [11.37%]	0.0026	109.93±15.46 [84-139]	15.77±12.95 [16.74%]	<0.001
7	118.33±23.96 [70-179]	22.50±24.40 [23.48%]	<0.001	117.00±17.89 [82-147]	22.83±14.56 [24.25%]	<0.001
12	119.37±17.15 [86-152]	23.53±17.01 [24.56%]	<0.001	120.37±18.17 [87-153]	26.20±15.05 [27.82%]	<0.001

In group PS there was a significant increase in BSL from basal value from 5th hour onward and it remained increased thereafter throughout the study period. The maximal blood sugar level was observed at 12 hours (119.37±17.15mg%; P value <0.001).

Similarly in group TS there was a significant increase in BSL as compared to the basal value, from 3rd hour onward and it remained increased thereafter. The maximal blood sugar level was observed at 12 hours (120.37±18.17mg%; an increase of 26.20±15.05mg% i.e. 27.82% from basal value; P value <0.001).

SERUM SODIUM LEVEL

Table 2 Mean serum sodium level (± S.D.) and minimum and maximum value at various time intervals and Mean change in serum sodium level (± S.D.) in mEq/L from the baseline (0hrs)

Observation time(hrs)	Group-PS (6%HES200/0.5)			Group-TS (6%HES130/0.4)		
	Mean± S.D.	Mean change ± S.D. (% variation)	P value (sig.)	Mean± S.D.	Mean change ± S.D. (% variation)	P value (sig.)
0 (Basal)	138.97±4.44 [130.6-148.6]			140.23±5.30 [131.1-152.6]		
1	139.03±2.79 [132.8-145.1]	0.06±5.08 [0.04%]	0.9517	139.93±2.97 [130.2-145.2]	-0.30±5.01 [-0.21%]	0.748
3	138.73±3.16 [132.7-145.9]	-0.24±5.41 [-0.17%]	0.8125	140.16±3.38 [131.4-149.5]	-0.07±6.23 [-0.05%]	0.9491
5	140.02±3.16 [131.2-145.7]	1.05±6.27 [0.76%]	0.3653	140.31±3.60 [133.6-149.4]	0.08±6.76 [0.06%]	0.9488
7	138.51±3.25 [130.4-143.8]	-0.46±4.99 [-0.33%]	0.6177	138.06±2.76 [130.6-142.5]	-2.17±6.20 [-1.55%]	0.0649
12	137.81±3.08 [130.7-143.7]	-1.16±5.35 [-0.83%]	0.2443	138.47±2.93 [132.4-147.6]	-1.76±5.62 [-1.25%]	0.0977

Mean change in serum sodium level from basal value in both the groups ranged from -2.17±6.20mEq/L to 1.05±6.27mEq/L. No significant deviation in the serum sodium level from basal value was observed. (P value >0.05)

SERUM POTASSIUM LEVEL

Table 3 Mean serum potassium level (± S.D.) and minimum and maximum value at various time intervals and Mean change in serum potassium level (± S.D.) in mEq/L from the baseline (0hrs)

Observation time(hrs)	Group-PS (6%HES200/0.5)			Group-TS (6%HES130/0.4)		
	Mean± S.D.	Mean change ± S.D. (% variation)	P value (sig.)	Mean± S.D.	Mean change ± S.D. (% variation)	P value (sig.)
0 (Basal)	4.69±0.90 [2.94-6.48]			4.76±0.78 [3.14-5.99]		
1	4.18±0.86 [2.97-5.83]	-0.51±0.69 [-10.83%]	0.0003	4.22±0.62 [3.08-5.46]	-0.53±0.69 [-11.20%]	0.0002
3	4.35±0.88 [2.67-5.79]	-0.33±0.84 [-7.10%]	0.0379	4.25±0.54 [3.42-5.59]	-0.51±0.83 [-10.67%]	0.0024
5	4.04±0.76 [2.75-5.62]	-0.65±0.71 [-13.78%]	<0.001	4.01±0.57 [3.19-5.86]	-0.74±0.79 [-15.63%]	<0.001
7	3.83±0.81 [2.68-5.84]	-0.86±0.77 [-18.32%]	<0.001	3.67±0.73 [2.84-5.67]	-1.09±0.94 [-22.87%]	<0.001
12	3.68±0.71 [2.41-5.38]	-1.01±0.87 [-21.54%]	<0.001	3.50±0.49 [2.66-4.64]	-1.26±0.81 [-26.43%]	<0.001

In both the groups there was a continuous and statistically significant decline in mean serum potassium level compared to basal value. By 12 hours mean serum potassium level decreased by 1.01 mEq/L in group PS and 1.26 mEq/L in group TS. This decrease was 21.54%, and 26.43% respectively. In both the group serum potassium level remained below the basal value throughout the study period.

SERUM CHLORIDE LEVEL

Table 4 Mean serum chloride level (± S.D.) and minimum and maximum value at various time intervals and Mean change in serum chloride level (± S.D.) in mEq/L from the baseline (0hrs)

Observation time(hrs)	Group-PS (6%HES200/0.5)			Group-TS (6%HES130/0.4)		
	Mean± S.D.	Mean change ± S.D. (% variation)	P value (sig.)	Mean± S.D.	Mean change ± S.D. (% variation)	P value (sig.)
0 (Basal)	101.95±4.56 [95.2-115.5]			102.60±2.96 [97.4-108.6]		
1	101.33±4.17 [95.3-114.9]	-0.62±3.69 [-0.60%]	0.3673	101.72±2.89 [96.6-108.8]	-0.89±3.83 [-0.87%]	0.2147
3	101.72±3.38 [95.8-112]	-0.23±5.20 [-0.23%]	0.8102	100.67±2.79 [95.6-109.5]	-1.93±4.15 [-1.88%]	0.0164
5	101.53±3.75 [96.2-112.7]	-0.41±4.74 [-0.41%]	0.6362	100.56±2.23 [95.3-105.4]	-2.04±3.84 [-1.99%]	0.0068
7	101.36±3.40 [95.4-110.1]	-0.58±4.09 [-0.57%]	0.4405	101.35±2.49 [95.4-106.4]	-1.25±3.33 [-1.22%]	0.049
12	100.61±3.51 [95.2-111.2]	-1.34±4.95 [-1.31%]	0.1492	100.51±2.29 [96.1-104.8]	-2.10±3.48 [-2.04%]	0.0026

Mean serum chloride level varied in the range of -2.10 to -0.23 mEq/L from baseline value. This difference was clinically & statistically not significant most of the time.

SERUM CALCIUM LEVEL

Table 5 Mean serum calcium level (± S.D.) and minimum and maximum value at various time intervals and Mean change in serum calcium level (± S.D.) in mg% from the baseline (0hrs)

Observation time(hrs)	Group-PS (6%HES200/0.5)			Group-TS (6%HES130/0.4)		
	Mean± S.D.	Mean change ± S.D. (% variation)	P value (sig.)	Mean± S.D.	Mean change ± S.D. (% variation)	P value (sig.)
0 (basal)	9.15±1.00 [6.86-10.85]			9.27±0.76 [7.91-10.67]		
1	8.39±1.11 [6.01-10.07]	-0.76±0.76 [-8.32%]	<0.001	8.70±0.91 [6.78-10.37]	-0.57±0.70 [-6.13%]	0.0001
3	8.34±1.33 [6.11-10.93]	-0.81±1.02 [-8.88%]	0.0001	8.77±1.26 [6.13-11.5]	-0.50±1.03 [-5.40%]	0.0123
5	8.32±1.42 [5.76-10.42]	-0.84±1.11 [-9.12%]	0.0003	8.64±1.32 [5.71-10.99]	-0.64±1.01 [-6.85%]	0.0017
7	8.4±1.32 [4.99-10.36]	-0.75±1.11 [-8.21%]	0.0009	8.72±1.18 [6.36-10.57]	-0.55±1.01 [-5.97%]	0.0056
12	8.72±1.27 [6.26-10.88]	-0.43±1.20 [-4.72%]	0.0579	8.94±1.15 [6.14-10.6]	-0.34±1.16 [-3.62%]	0.1243

In both the groups there was continuous decline in Mean serum calcium level from basal value throughout the study period. By 12 hours it decreased by 0.43 mg% and 0.34 mg% from baseline i.e. 4.72% and 3.62% in group PS and TS respectively. Group PS exhibited the fall in a large number of patients.

In our study comparatively less decrease was found in tetrastarch group (6% HES-130) i.e. 3.62%.

4. DISCUSSION

The commercially available artificial colloid Hydroxyethylstarch (HES) is very effective plasma expander and is widely used to compensate blood loss in 1:1 ratio.

The artificial colloid Hydroxyethylstarch (HES) is available in different types according to their concentration, molecular weight, source of starch (waxy maize derived or potato starch derived) and their carrier solution (normal saline or balanced salt solution). The older HES products were associated with adverse effects like pruritus,coagulopathy,platelet dysfunction, elevated serum amylase level, hemodilution, renal dysfunction, hyperbilirubinemia, hearing loss, tissue accumulation etc.So they evolved over time retaining their volume efficacy with improved safety and pharmacological profile. Reduction in molecular weight led us to newer third generation HES with shorter half life, improved pharmacokinetic and pharmacodynamics properties and lesser side effect[1,2].

After an IV infusion smaller HES molecules (less than renal threshold ie 45-60 kDa) are excreted and bigger molecules are enzymatically metabolized into smaller molecules until the renal threshold for excretion is reached. HES with low Molecular Substitution are broken down more rapidly to produce greater concentration of oncotically active particles. Part of HES diffuses into interstitial space, redistributed and ultimately eliminated and other is taken up by the reticuloendothelial system and broken down slowly. Thus, the degree of plasma and tissue accumulation is highly dependent on structure, the specific HES type, and its physicochemical properties. HES with high molecular weight are associated with more side effects[1,2.]

So this study was planned to evaluate effect of pentastarch and tetrastarch on blood sugar level and serum electrolyte level in gynaecological surgeries.

4.1 BLOOD SUGAR LEVEL

There was a steady rise in the blood sugar level in both the groups. BSL did not return to basal value even up to 12 hours. The mean rise (cf. to basal value) in the blood sugar level after 12 hours, 6% Pentastarch group, and 6% Tetrastarch group was 23.53±17.01 mg % (24.56%), & 26.20± 15.05mg% (27.82%) respectively. A substantial increase in BSL was witnessed in both group but with in physiological limit.

The result of our study were supported by R. Beyer et al[3], Soumya Sankar Nath et al[4], Raghu R et al[5], Ki Tae Jung et al[6], Patki A et al[7] while study done by Norbert H. Vogt et al[8] , DrShailesh S. Murty et al [9] donot support our study Thus it is evident that the breaking of the HES molecule to glucose is delayed in pentastarch compared to tetrastarch. The increase in glucose level although statistically significant was thought not to be clinically relevant in all these patients. In the diabetic patients, peripheral disposal of lactate may be impaired because of inactivation of pyruvate dehydrogenase, while gluconeogenesis will be enhanced simultaneously. Thus in diabetic patients, lactate will be converted to glucose causing marked hyperglycemia although this does not hold true in non-diabetics to the same extent. In the non diabetics also, an increase in blood sugar level was found. Lactate can also be used as an oxidative fuel in extra hepatic tissues.

4.2 SERUM SODIUM LEVEL

There was no significant Mean change in serum sodium level from basal value in any group throughout the study period. The variation ranges from -2.17 to +1.05 mEq /L from basal value.

A study done by Norbert H. Vogt et al[8] (1996), R. Beyer et al[3] (1997), G. B. Lehmann et al[10] (2007) showed there were no change in the serum electrolytes (Na+, K+&Cl-) in the time course of study period. Our study results for serum sodium are similar to these studies.

Wilkes NJ et al[11] (2001) and Brahma SK et al[12] (2017) in their study with use of balanced versus saline based HES and crystalloid solution perioperatively found no significant changes in serum sodium level in both the group. So these result further supported our study.

4.3 SERUM POTASSIUM LEVEL

In both the groups there was a steady decline in mean serum potassium level from basal value. By 12th hour mean serum potassium level decreased by 1.01 mEq/L in group PS, and 1.26 mEq/L in group TS. In both the study groups, serum potassium level remained below basal value throughout the study period. It might be due to dilutional effect produced by HES which draws water intravascularly.

The mean values of serum potassium were within the physiologic range through the study period and the clinical progress throughout the surgical course remained uneventful.

BogumilaWoloszczuk-Gebicka (2006)[13] supported our study while studies by Norbert H. Vogt et al[8] (1996) R. Beyer et al[3] (1997), G. B. Lehmann et al[10] (2007), Wilkes NJ [11] (2001) et al and Brahma SK et al[12] (2017) have different results. It might be due to difference in volume of HES used, duration of the study period and use of arterial blood for sampling.

4.4 SERUM CHLORIDE LEVEL

Mean serum chloride level varied in the range of -2.10 to -0.23 mEq/L from baseline value. In group TS there was a statistically significant (P value <0.05) change in Mean serum chloride level from 3rd hour onwards but the mean values were well within the physiological limits. Sodium chloride is often administered because it is isotonic with plasma and is initially distributed in the extracellular compartment. Non physiologic levels of chloride however have been linked to the development of metabolic acidosis and the possible impairment of splanchnic perfusion as judged by the abdominal discomfort and reduced urine output.

In our study, changes in serum sodium and chloride level are nonsignificant, which might be due to combined effect of HES produced dilutional effect and normal saline as its carrier solution.

Norbert H. Vogt et al[8] (1996) and G. B. Lehmann et al[10] (2007), supported our study while studies by Bogumila Woloszczuk-Gebicka[13] (2006) and Wilkes NJ [11] (2001) showed hyperchloridemia in their studies.

Wilkes NJ et al[11] (2001) and Brahma SK et al[12] (2017) in their study with use of balanced versus saline based HES and crystalloid solution perioperatively found significant changes in serum chloride level ie hyperchloridemia in saline based solution group.

Use of balanced salt solution RL throughout study period after initial preloading with saline based HES might explain minimal variation in serum chloride level. Wilkes NJ et al[11] and Brahma SK et al[12] also found significant variation in saline based groups rather than in balanced group.

4.5 SERUM CALCIUM LEVEL

In group PS there was highly significant (P value<0.001) decrease in serum calcium level from baseline value till 7th hours but then it became statistically non significant (P value>0.05) at 12 hours. In group TS there was statistically significant (P value<0.05) decrease in serum calcium level at 3rd& 7th hour. It was highly significant (P value<0.001) at 1st hour & non significant (P value>0.05) at 12th hour. R. Beyer et al[3] (1997) compared HES and Gelatin in 48 patients of orthopedic surgery serum calcium Values in the HES group remained significantly low for up to 12 hours (7.8±0.7mg %) after operation. At 24 hours postoperatively it was 8.1±0.4mg%. Our results also correlate very well with this study.

Wilkes NJ et al[11] in their study with use of balanced versus saline based HES and crystalloid solution perioperatively found highly significant (p value 0.0001) decrease in serum calcium level in both the group.

The decrease in total serum calcium in both the groups can be explained by the known "rule of thumb" whereby a decrease in albumin concentration of 1g/dl is accompanied by a decrease in total serum calcium of 0.8mg/dl. However, Studies by Vogt, Schönberger and Kilian[14] have confirmed that HES does not specifically affect ionized calcium even at higher doses.

Again this significant fall in serum pottasium and calcium level might be due to dilutional effect of HES and absence of pottasium and calcium in carrier solution.

5. CONCLUSION

The administration of Hydroxyl ethyl starch produces a rise in blood sugar level to a variable degree according to the concentration and extent of substitution but with in physiological limit.

There is no appreciable effect on serum sodium and chloride level after its administration. There is a marked drop in serum calcium and potassium in both the groups which was evident even up to 12 hours. 6% tetrastarch 130 produces the less disturbances in serum calcium and serum potassium level.

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