Research Report

Effect of Administering Enteral Nutrition pre Caesarean Section Towards High Sensitivity C-Reactive Protein Levels

Efek Pemberian Nutrisi Enteral Pra Sectio Caesarea terhadap High Sensitivity C-Reactive Protein

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Abstract

Objective: To determine the effect of enteral nutrition pre caesarean section (CS) on high sensitivity C-Reactive Protein (hsCRP) serum levels post CS.

Method: This clinical trial study on elective CS patients with lumbal anesthesia, was done to compare hsCRP levels two hours pre and 48 hours post CS between the treatment group (P) who was given 200 ml enteral nutrition per oral and control group (K) received 200 ml sweet tea two hours pre CS. The study was already approved by the Ethical Clearance Research Committee of Faculty of Medicine University of Indonesia.

Results: Twenty seven elective CS patients in Rumah Sakit Umum Daerah (RSUD) Bekasi were selected using certain criteria and divided into two groups using block randomization. Data collected included age, gestational age, nutritional status, indication, of CS total blood volume, and duration of CS, as well as energy intake of energy and protein. Laboratory hsCRP serum levels were examined two hours pre and 48 hours post CS. Statistical analysis were performed using t-test and Mann-Whitney, with 5% level of significancy. Twelve subjects in each P and K group, completed the study respectively. The mean of age was 30.08 ± 4.01 years. The nutritional status based on upper mid arm circumference in both groups was normal, while using *kartu menuju sehat* (KMS) in all of subjects were classified as overweight. The characteristic of the two groups closely matched at base line ($p > 0.05$). There was increased hsCRP serum at post CS which was higher in the K group and statistically significant ($p = 0.00$).

Conclusion: Administration of 200 ml enteral nutrition two hours pre CS is associated with a reduction of 48 hours post CS hsCRP serum level compared with sweet tea.

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Keywords: elective CS, enteral nutrition pre CS, hsCRP serum concentration

Abstrak

***Tujuan**: Mengetahui pengaruh pemberian nutrisi enteral per oral pra SC terhadap kadar serum high sensitivity C-Reactive Protein (hsCRP) pasca SC.*

***Metode**: Penelitian ini merupakan uji klinis pada ibu hamil yang direncanakan melahirkan secara SC dengan anestesi lumbal, untuk membandingkan kadar hsCRP serum dua jam pra dan 48 jam pasca SC pada kelompok perlakuan (P) yang mendapat nutrisi enteral per oral 200 ml dibandingkan dengan kelompok kontrol (K) yang mendapat larutan teh manis 200 ml, yang diberikan dua jam pra SC. Penelitian ini telah disetujui komisi etik penelitian Fakultas Kedokteran Universitas Indonesia.*

***Hasil**: Sebanyak 27 pasien bedah sesar berencana di Rumah Sakit Umum Daerah (RSUD) Bekasi yang memenuhi kriteria penelitian dibagi dalam dua kelompok secara randomisasi blok. Data yang dikumpulkan meliputi usia, usia kehamilan, status gizi, indikasi SC, lama SC, jumlah perdarahan, dan asupan energi dan protein. Pemeriksaan kadar serum hsCRP dilakukan dua jam pra SC dan 48 jam pasca SC. Uji statistik yang digunakan adalah uji t dan uji Mann-Whitney dengan batas kemaknaan 5%. Sebanyak 12 orang kelompok P dan 12 orang kelompok K dengan rerata usia 30,08 ± 4,01 tahun mengikuti penelitian secara lengkap. Status gizi seluruh subjek berdasarkan pengukuran lingkar lengan atas (LiLA) termasuk kategori gizi baik, sedangkan berdasarkan kartu menuju sehat (KMS) ibu hamil termasuk kategori gizi lebih. Pada awal penelitian, karakteristik data dasar pada kedua kelompok tidak memperlihatkan perbedaan yang bermakna ($p > 0,05$). Pada akhir penelitian terdapat peningkatan kadar serum hsCRP pasca SC yang lebih tinggi pada kelompok K dan secara statistik bermakna ($p = 0,00$).*

***Kesimpulan**: Pemberian 200 ml nutrisi enteral dua jam pra SC dapat mengendalikan peningkatan kadar serum hsCRP 48 jam pasca SC dibanding kelompok kontrol.*

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***Kata kunci**: SC elektif, nutrisi enteral pra SC, kadar serum hsCRP*

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INTRODUCTION

Caeserean section (CS) is an alternative way for birth delivery process carried out when vaginal delivery is not possible.[1] Like other surgical procedures, in general, the effect of CS is the increasing possibility of post surgery inflammation process. In patients with those conditions if they do not receive adequate medical and nutritional treatments, the likelihood of post surgery complications such as delay healing and sepsis may occur.[2] The degree of inflammation response which could occur depends on several factors such as gestational age, nutritional status, surgical indications, procedure and duration of surgery, blood volume pre and post surgery, duration of pre surgery fasting, as well as nutritional intake both pre and post surgery.[3,4]

These problems commonly occur during every surgical procedure and they may precipitate oxidative stress responses that may cause disruption in cytokine balances ie pro-inflammatory cytokines will increase whereas anti-inflammatory cytokines will decrease, and thus induce generation of catabolic protein process that may elevate acute phase protein synthesis such as C-Reactive Protein (CRP).[3,4]

These increased of CRP levels may reach until 1000-times bigger from normal values and this may occur within 48 - 72 hours post trauma/surgery; this condition demonstrates the occurence of a significant inflammation process as well as severe acute catabolic process.[5] Other factors which influence CRP levels are pregnancy, several chronic diseases (such as diabetes mellitus (DM), hypercholesterolemia), and consumption of certain drugs. Besides those factors, obesity, acute/chronic infection and smoking habits may also increase CRP levels.[5,6]

Regional anaesthesia techniques and shorter pre surgery fastings,[7] have shown an important role in controlling inflammatory responses and post surgery catabolic processes post surgery.[8] In adult patients, the guideline for pre surgery fasting recommended by *Ikatan Dokter Spesialis Anestesiologi dan Reanimasi Indonesia (IDSAI)*[9] is to give water three hours before surgery. At *Rumah Sakit Umum Daerah (RSUD) Bekasi,* patients are asked to fast for 8 - 12 hours before CS.[10] Pre surgery fasting is intended to empty the stomach, in an attempt to reduce the risk of aspiration, while a study showed that gastric-emptying in third-trimester pregnant women who received enteral nutrition less than that two hours had the same condition with subject who drank water.[11]

One study showed that long duration of pre surgery fasting (> 12 hours) will increase post surgery inflammatory responses post surgery and worsen the patient's condition,[12] as shown by De Villers et al[13] Cicarelli et al[14] found significantly higher CRP and Serum Amyloid A (SAA) levels post elective CS patients which were asked to fast for more than six hours compared to those with normal delivery.

This clinical trial was aimed to compare between 200 ml enteral nutrition per oral (P group) and 200 ml sweetened (K group) which was given two hours pre CS on the level of hsCRP 48 hours post CS, among lumbal anesthesia elective CS subjects.

SUBJECT AND METHOD

Subject

The study was carried out at the obstetrics and gynecology Department of RSUD Bekasi from August to November 2009. This study has been approved by the Committee of The Medical Research Ethics of Faculty of Medicine University of Indonesia. Informed was obtained consents from 27 patients. Subjects were randomized by sealed envelope (block randomization) to one of two groups. Twenty four subjects out of 27 patients (88.8%) had completed this study. Two subjects were considered as drop out as they refuse to have their blood obtained 48 hours post-CS and one subject had blood lysis.

The inclusion criteria for subjects were: 1) single pregnancy, 2) gestational age > 37 weeks, while the exclusion criteria were 1) known to have an on-going infection, 2) random blood glucose pre CS ≥ 200 mg/dl,[15] 3) total cholesterol level ≥ 240 mg/dl,[16] 4) impairement of liver function (SGOT/PT ≥ 38 U/l / 41 U/l),[17] 5) consumed Non Steroid Anti Inflamatory Drugs (NSAIDs)/aspirin/corticosteroids and/or cholesterol-lowering drugs.[5]

The treatment group (P group) was given enteral nutrition per oral and control group (K group) received sweetened two hours before CS respectively. Sample size was calculated using formula for randomized clinical trial,[18] the total sample required for each grop was calculated based on the abilitity to differentiate hsCRP level of two groups. Using 4.5 mg/dl as the mean difference and 4.2 mg/dl[14] as the standard deviation with α 0.05 and power of the study equal to 80%, a minimum sample size of 14 subjects was considered adequate for each groups.

Study Measurements

Data were acquired from interviews, anthropometric measurements for assesing nutritional status using *Kartu Menuju Sehat* (KMS) from the Indonesian Ministry of Health for pregnant woman[19] and upper arm circumference,[20] Dietary assessment using food record[21] pre and 2x24 hours post CS, and were analysed using Nutrisurvey 2007. In addition, laboratory test for two hours before and 48 hours hsCRP serum after CS using Immunoflowmetry hsCRP Assay based on BN system.[22] Subject recruited consecutively.

Statistical Analysis

Statistical analysis was carried out using the Statistical Package for Social Science (SPSS) programme version 11.5 software. For data which were normally distributed, data were presented as mean±standard deviation, otherwise data were presented as median figure (minimum-maximum). The normallity test assesed by Shapiro-Wilk test. Differences in mean value were assesed by t-test for the normal distributed data or Mann-Whitney for data which were not normally distributed.

RESULT

The mean age of the subjects was 30.08 ± 4.01 years, 45% was 31 - 35 years old. The median range of gestational age was 38 weeks (37 - 41 weeks). The most indication of CS (50%) was previous CS. Based on of upper arm circumference, all of the subjects were categorized as good nutritional status, whereas based on KMS all of the subjects were classified as overweight.

Table 1. Distribution of subject based on duration of surgery, blood volume, and nutritional intake pre CS.

Variable	Treatment (n = 12)	Control (n = 12)	p value
Duration of operation (minute)	40 (25 - 48)	36.5 ± 5.28	0.443
Blood volume (ml)	251.11 ± 91.94	286.25 ± 89.81	0.858
Energy intake (kcal)	1867.38 ± 123.64	1819.42 ± 120.64	0.428
% energy intake/TER	90.96 ± 6.97	87.87 ± 4.46	0.768
Protein intake (gram)	74.14 ± 15.48	74.78 ± 12.88	0.913
% Protein intake/TER	16.03 ± 3.85	16.60 ± 3.51	0.706

TER = total energy requirement

The characteristics data of the two groups at base line were not significantly different, therefore the two groups were closely matched at base line.

Table 2. Energy and protein intakes post CS.

Variable	Treatment (n = 12)	Control (n = 12)	p value
Energy			
Intake (kcal/day)	1842.84 ± 50.83	1817.80 ± 33.56	0.167
TER Post CS (kcal/day)	2404.03 ± 130.83	2418.68 ± 107.44	0.768
% energy intake/TER	76.93 ± 5.73	74.29 ± 3.66	0.413
Protein			
intake (g/day)	75.43 ± 4.94	76.45 ± 3.77	0.110
% intake/TER	16.11 ± 1.13	16.81 ± 0.93	0.134

TER = total energy requirement

The percentage of average energy intake compared to TER in both groups were less than requirement (< 80%), and did not show a significant difference. The percentage of average energy and protein intake compared to TER in both groups were adequate (10 - 20%), and did not show a significant difference.

Table 3. Mean serum of hsCRP levels pre and post CS.

Variable	Treatment (n = 12)	Control (n = 12)	p value
hsCRP Pre CS	3.30 (0.20 - 18.30)	3.30 (1.30-20.30)	0.478
hsCRP Post CS	40.17 ± 18.68	78.45 (50.20-192.00)	0.00*

**significant*

The median value of serum hsCRP two hours pre-CS between both groups was not significantly different, but there was increase in 48 hours post-CS level in the K group and statistically significant (p = 0.00).

DISCUSSION

Limition of this study was that the determination of nutritional status using the measurements of upper-arm circumferences and KMS. Base on upper-arm circumference, the nutritional status was only categorized into poor and good nutritional status,[19] whereas base on KMS the nutritional status was divided into poor, good, and overweight[20] (no classiffication for obese). Determination of nutritional status would be more accurate if the subject's nutritional status was known before they were pregnant.

Counfounding variables in this study including infection, random blood glucose pre CS, total cholesterol, impairement of liver function and consumed Non Steroid Anti Inflamatory Drugs (NSAIDs)/aspirin/corticosteroids and/or cholesterol-lowering drugs were controlled by restriction using exclusion criteria so the result was not bias.[23] The characteristic data of the two groups as well as hsCRP level at baseline was not significantly different. We may conclude that the difference in the result is caused by the treatment given.[23]

The mean age was 30.08 ± 4.01 years and the median gestational age of the subjects was 38 weeks (37 - 41 weeks). This condition was similar compared with data from a private hospital in Surabaya, which showed the median age of CS patients was 21 - 30 years and the median gestational age was 38 - 42 weeks.[24] A study done by De Meuss et al[25] showed a correlation between gestational age and increasing of CRP levels in pregnant women, where gestational age < 37 weeks as well as > 42 weeks showed increament in CRP levels.

The highest percentage (50%) of indication for elective CS in this study was previous CS. This was in concordance with the data of CS cases in Surabaya Private Hospital, where most of the CS was also due to previous CS.[24] However, data from RSUD Bekasi showed that the most indication of elective CS was early disruption of amniotic fluid.[26] One of the risk factors which could increased inflammatory response and post-CS infection was early disruption of amniotic fluid. Two subjects in this study with PROM (Premature Rupture of Membrane) showed higher pre CS hsCRP levels (> 10 mg/l). A study by Cicareli et al[14] found higher levels of CRP post CS amongst PROM. This was related with the possibility of the occurence of intrauterine infection.

The duration of operation in this study in group P was 40 (25 - 48) minutes whereas in group K was 36.5 ± 5.28 minutes. There was no significant difference between both groups (p = 0.443). Duration of operation is one factor influencing inflammatory response after surgery.[27] Visser[1] found a correlation between the duration of surgery more than three hours with the increasing CRP levels post surgery.

In terms of inflammatory response post surgery, first hemorrhage (> 750 ml). The mean of blood volume during CS in group P was 251.11 ± 91.94 ml whereas in group K was 286.25 ± 89.81 ml, and no significant difference (p = 0.858). According to American College of Surgeons, a blood volume during surgery < 750 ml is categorized as less, and this leads to a slighter inflammatory response.[28] Second, energy intake. Energy intake in both groups was not significantly different both pre and post CS, the mean energy intake percentage when compared to TER pre CS in each group was categorized as sufficient (80 - 120% TER). A sufficient energy intake will fulfill total daily energy requirements, and prevent excessive inflammatory responses.[29] European Society of Parenteral and Enteral Nutrition (ESPEN) recomended that energy intake which equivalent to TER may prevent severe inflammatory response post surgery.[30] Energy intake pre surgery serves as energy storage which could be used for the increasing need of energy caused by the surgery process, as well as to prevent excessive catabolism of tissues due to the surgery stress.[31]

Our study had a limitation in term of dietary assesment. The mean percentage of energy intake compared to TER post CS in each group was less than adequate (75% TER). A higher need of energy in this study could be also related to the determination of TER, used the Harris Benedict (HB) formula.[32] Using HB formula energy requirement consists of basal energy rate (BER), stress factor and level of physical

activity. An overestimated as well as underestimated calculation could be happened.

Protein intake was an important factor for body protein synthesis such as formation of immune cells and acute phase proteins which control inflammation and metabolic stress responses due to surgery trauma. Percentage of protein intake pre CS in both groups were categorized as sufficient (10 - 20% TER). A study by Casas-Rodera et al[33] in orthopaedic patients receiving adequate protein intake pre and post surgery (± 15% TER) revealed lower post surgery CRP levels.[34] Several studies showed the correlation between serum CRP and several nutritional components ie protein component (arginin, glutamin) and fatty acid (omega 3, omega 6) which could lower hsCRP level.[37] The median of pre CS hsCRP levels between both groups was not significant difference ($p = 0.478$). This result was in concordance to a study by Wood et al[35] which showed that the median level of CRP in pregnant women was 3.64 mg/l (1.49 - 12.6 mg/l). An increase of CRP level in pregnant women was correlate with the increase of body fat during pregnancy and this condition induces the increase of leptin hormones which trigger the increase of CRP production by liver cells.[36]

A significant difference of serum hsCRP levels post CS was found, which K group showed significantly higher serum hsCRP levels that P group (Table 3). This illustrates a lower inflammatory response in P group compared with K group.

A study by Wu et al[38] on post surgery gastrointestinal cancer patients showed a significant different decrease of serum CRP level as also showed in P group who received enteral nutrition enriched with immunonutrition (glutamin, arginin, and omega-3 fatty acid) compared to K group whose received the standard formula. De Luis et al[39] has also shown that amongst head and neck cancer patients whose received enteral nutrition which fortified with arginin and omega-6 fatty acid, had a lower CRP level compared to the control group.

Glutamin is an amino acid known to play a role in preventing body protein catabolism, and may also resource in then formation of immune cells as well as accelerating wound healing. Glutamin also maintains immune functions by controlling production of pro-inflammatory cytokines.[37] This was proven by a study from Tang et al[40] which showed a significant decrease in IL-2 cytokine and CRP levels post surgery among subjects who received parenteral nutrition enriched with glutamin.

Various studies regarding supplementation of arginin in combination with omega-3 showed both components act as anti-inflammatory agents. In colorectal cancer patients, Braga et al[41] found a decreasing in CRP level post surgery when given enteral nutrition enriched with arginin and omega-3. The combination of arginin and omega-3 may supress prostaglandin production and pro-inflammatory cytokines, which decrease the production of acute phase proteins. The combination is also thought to increase immune response (macrophage and Natural Killer cell), as well as proliferation of cell-T.[37]

CONCLUSION

Administration of 200 ml enteral nutrition two hours pre CS is associated with the reduction of 48 hours post CS hsCRP serum level compared with sweetened ($p = 0.00$).

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