Brief Communication

Apnea after reversal of neuromuscular blockade. A case of rare mix-up

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Medication error is one of the leading causes of morbidity and mortality in hospitalized patients. Considering the potency, types, and frequency of the drugs administered to patients undergoing anesthesia, the potential exists for errors with disastrous consequences. Several studies indicate that the incidence of medication error associated with anesthesia practice is common. Analysis of critical incidences by Cooper and colleagues showed that drug-related events far exceeded the next most common problem, disconnection of the breathing circuit. The Australian Incident Monitoring Study analyzed adverse events during anesthesia and reported that “The wrong drug” was the most common adverse event. Indeed, anesthetic drug errors have been reported for every aspect of anesthetic–related care, most common being the “Syringe swaps” (70.4%) and misidentification of the label (46.8%). An analysis of closed malpractice claims showed that medication issues are a leading cause of malpractice litigation against Canadian anesthesiologists, totalling 3.5% of claims against all physicians from 1998 to 2002. The most common cause of malpractice action was a medication-related event. Berman reported that errors due to look-alike or sound-alike medication names are common in the United States. Up to 25% of all medication errors are attributed to name confusion, and 33% to packaging or labeling confusion. Systems and recommendations have been developed that may reduce the occurrence of such errors. In our case, an ASA I, male child of 4 years of age and 15 kg body weight was posted for repair of left inguinal hernia under general anesthesia. His routine complete blood count, and biochemistry including urine analysis were within normal limits. The child was premedicated with 5 ml promethazine hydrochloride oral syrup 1 hour before induction of anesthesia. In the operating room, before initiation of anesthesia, his vitals were recorded, his heart rate was 110/minute with normal sinus rhythm, his blood pressure was 106/70 mm Hg and arterial saturation was 99%. An intra-venous cannulation was performed with 22 G cannula without any difficulty and 5% dextrose with one-quarter normal saline started. Anesthesia was induced with 60 mg thiopentone sodium and relaxed with 20 mg suxamethonium, and tracheal intubation was performed with 4.5 mm uncuffed endotracheal tube. Anesthesia was maintained with 25 µgm fentanyl, 50% oxygen with nitrous oxide, 0.6-0.8% sevoflurane and atracurium besylate 0.5 mg/kg as, and when required.

Ayre’s T Piece circuit was used for intermittent positive pressure ventilation. Surgery lasted for 45 minutes, and the whole course of anesthesia was uneventful. At the end of surgery, he gained spontaneous respiration, and was kept on 100% oxygen only. Neuromuscular blockade was reversed with 0.75 mg neostigmine and 0.2 mg atropine. After reversal, the heart rate came down from 102/minute to 55/minute and he gradually developed apnea. Heart rate was corrected with the use of atropine. The cause of this fall in heart rate and apnea could not be detected. This unexpected result of reversal alerted us to consider a medication error. A careful check of the syringes loaded with drugs revealed atracurium besylate mixed with neostigmine methyl sulphate instead of atropine. Two syringes kept side-by-side one loaded with atracurium besylate, 5 mg/ml and marked “Atra” and the other syringe loaded with atropine sulphate, 0.1 mg/ml marked “Atro”. In this case, 0.75 mg of neostigmine was mixed with 10 mg of atracurium besylate instead of 0.2 mg of atropine sulphate. The manner in which labeling of the syringes was carried out, could have happened with anyone involved in the anesthetic care of the patient. In this patient, this “mix-up” did not cause any undesirable side effect except prolong apnea and bradycardia, which were taken care of appropriately. Later, when the effect of the muscle relaxant wore off, an appropriate dose of reversal was used and tracheal extubation carried out. He was observed for one hour in recovery and then shifted to the ward without any problem. Though this medication error did not cause any deleterious effect on the patient’s health, it definitely indicates the need for improved standards for drug labeling.

To conclude, the utmost care is essential while giving drugs during anesthesia care. To improve patient safety, each medical and surgical discipline needs to identify the sources of error and develop evidence based preventative strategies. The incidence of medication error during anesthesia is uncertain, but it is astonishingly low given the millions of drugs administered during anesthesia care.

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References


Paeonol inhibits the proliferation of human colorectal carcinoma cells and synergic with chemotherapeutic agents

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Colorectal cancer is the third most common cancer in the world and the second leading cause of cancer-related deaths in the United States. Surgical removal of the tumor supplemented with chemotherapeutic agents is a major treatment for it. However, most of the chemotherapeutics for colorectal carcinoma have great aversive effects, so it is indispensable for us to find a proper and natural therapeutic strategy for our patient. Paeonol (Pae) is a Chinese traditional herb, which has been shown to exhibit anti-pyretic, sedative, anti-inflammatory and anti-bacterial activities. It was reported that Pae exhibited anti-tumor activity in multiple cancer cell lines. Gastric lavage with Pae could inhibit liver tumor growth in mice model. Paeonol has been proven to suppress hepatocellular tumorigenesis in vitro. However, little was known on the effect of Pae on colorectal cancer cells. We provided evidence here that Pae inhibited the growth of colorectal carcinoma cell line HT-29, which was also synergistic with certain chemotherapeutic drugs.

The current study was conducted at Renmin Hospital of Wuhan University in China, between September 2003 and September 2004. And the study was approved by our Hospital Ethics Committee. Human colorectal carcinoma cell lines HT-29 were purchased from Oncology Institute of the Zhongnan University. Paeonol was obtained from Shanghai first pharmaceutical factory while 5-fluoro-2,4(1H,3H)pyrimidinedione (5-FU) was from Xu Dong Hai Pu Pharmaceutical Co. Ltd, Shanghai, China, mitomycin C (MMC) from Tokyo Co., and diaminedichloroplatinum (c-DDP) from Qi Lu Pharmaceutical Co., Shandong, China. The in vitro growth rate of HT-29 cells treated with Pae, was measured by the methyl thiazolyl tetrazolium (MTT) method. Briefly, HT-29 cells (1×10⁴ cells/well) were seeded in 96-well plates. We added Pae to these cells in the concentration of 0.024, 0.047, 0.094, 0.188, 0.376, 0.752, 1.504 μmol.L⁻¹, respectively. And one group of cells was added without Pae as blank control. Making sure that each group contained 5 slots. Then the cells were incubated in an incubator for 24, 48, 72 and 96 hours. We added 20 μl MTT to each slot 4 hours ahead of termination, abscised the culture solution, and added 200 μl dimethyl sulphoxide (DMSO) to each slot again. The absorbance value was measured at a wavelength of 570 nm with background subtraction at 650 nm by the use of spectrophotometer. Inhibitory rate = (1-Ae/Ac)×100%. We also observed HT-29 cells at Log phase that had been incubated with different concentrations of Pae under inverted microscope. The cells were also cultured on cover-slip and fixed by 10% formalin and stained with hematoxylin and eosin. Each experiment was performed at least 2 times and results are presented as the mean ± standard deviation. The p values were determined by unpaired t test by using the Statistical Program for Social Sciences analysis. We found out that Pae significantly inhibited the growth of the HT-29 cells at a concentration of 7.81-250 mg/L in a dose-effect and time-effect pattern (Figure 1). Microscopically, the control cells proliferated faster with a larger size and brighter field than cells treated with Pae. Hematoxylin and eosin staining of the control cells showed blue nuclear staining without visible apoptotic body. Cells treated with Pae exhibited apoptotic cell in a concentration of 31.25-250 mg/L. Apoptotic cells were distinguished by the use of spectrophotometer.
Paeonol inhibits the proliferation of colorectal cancer

Table 1 - Paeonol synergizes with 3 chemotherapeutic drugs on the inhibition of HT-29 cell proliferation.

<table>
<thead>
<tr>
<th>Items</th>
<th>A</th>
<th>Inhibition rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.073 ± 0.021</td>
<td></td>
</tr>
<tr>
<td><strong>Single Use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pae</td>
<td>0.871 ± 0.013</td>
<td>(18.826)*</td>
</tr>
<tr>
<td>5-FU</td>
<td>0.751 ± 0.028</td>
<td>(30.002)*</td>
</tr>
<tr>
<td>MMC</td>
<td>0.749 ± 0.030</td>
<td>(30.151)*</td>
</tr>
<tr>
<td>DDP</td>
<td>0.745 ± 0.019</td>
<td>(30.569)*</td>
</tr>
<tr>
<td><strong>Combined use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pae+5-FU</td>
<td>0.280 ± 0.009</td>
<td>(73.884)*†</td>
</tr>
<tr>
<td>Pae+MMC</td>
<td>0.373 ± 0.025</td>
<td>(65.267)*†</td>
</tr>
<tr>
<td>Pae+DDP</td>
<td>0.497 ± 0.018</td>
<td>(53.713)*†</td>
</tr>
</tbody>
</table>

Concentration of Pae - 7.81 mg/L, 5-FU - 10 mg/L, MMC - 0.5 mg/L, DDP - 10 mg/L. *p<0.01; †p<0.001, 5-FU - 5-fluoro-2,4(1H,3H)pyrimidinedione, MMC - mitomycin C, DDP - dichlorodiammineplatinum.

Pae - Paeonol, A - absorbance value by the use of spectrophotometer.

nuclear condensation and fragmentation as well as deep nuclear staining. Furthermore, 7.81 ml/L of Pae was combined with or without one of 3 chemotherapeutic drugs (10 mg/L 5-FU, 0.5 mg/L MMC, or 10 mg/L c-DDP) to treat the cells. As a control, all drugs were also applied respectively. There was also a blank control. Forty-eight hours later, MTT assay was performed. We saw that low dose of Pae achieved a significantly synergistic effect with 5-FU, MMC or c-DDP in the inhibition of HT-29 cell growth (p<0.01). Paeonol had the most prominent synergistic effect with 5-FU (Table 1). Therefore, we came to the conclusion that, besides its direct anti-tumor activity, Pae might sensitize cancer cells to multiple chemotherapeutic drugs. Low dose of Pae (7.81 ml/L) could only inhibit HT-29 cell growth by 18.826%, whereas its combined use with 5-FU, MMC and c-DDP at a concentration of IC₁₀₀ achieved an inhibitory rate of 73.884%, 65.267% and 53.713%, respectively. The combined use of Pae with chemotherapeutic drugs was significant (p<0.01).

In conclusion, plant extract Pae possesses the anti-tumor and immunity-promoting activity with apparent side effects. We are expecting that combined application of Pae in the clinical treatment of colorectal cancer with 5-FU would enhance the efficacy of the chemotherapeutic drug with less side effects due to a reduced dose.

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References


Household cardiovascular health education. A school–based approach

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There is no doubt that control of risk factors is an effective strategy in primary prevention of cardiovascular disease. Lifestyle behaviors such as unhealthy diet and physical inactivity contribute significantly to the progression of cardiovascular disease. Cardiovascular health promotion in children has the potential to reduce the risk of atherosclerosis in both the children and their families. Schools provide an excellent setting for introducing comprehensive health education and promotion as a public health approach to the general population. Furthermore, it is suggested that involvement of families in school-based programs is feasible and effective.

Like many other countries, coronary heart disease (CHD) is the leading cause of mortality and morbidity in Iran. The process of urbanization and corresponding lifestyle changes has been associated with increase in the prevalence of CHD. On the other hand, the population of Iran is relatively young. This provides an opportunity to prevent cardiovascular disorders since childhood. As many people in Iran still do not have enough information on cardiovascular risk factors, we performed this school-based educational intervention to investigate its effect on the improvement of cardiovascular health knowledge in targeted households. The study was carried out on ordinary households of 1000 fifth-grade boys and girls.
After intervention.

differ from the pretest.

girls selected at random from schools within a single educational district of Tehran. Both the pre and post questionnaires had 48 questions, each of them has one score. The questionnaire was tested before embarking on the study. The children were considered as conduits of information and they were asked during the briefing session to encourage every member of their household to take an interest in the study and the educational material supplied. Then the children received the educational materials. They were also supplied with a trigger object (T-shirt), which they had to wear for as much as possible of the survey time that they spent with at least one member of their household. All members of the families were encouraged by their fifth-grader to study the material individually or together in proper time. The study period lasted 7 days from the date on which the material was handed to each child. Seven days after the handover date, each child received a post test questionnaire. The children took the questionnaires home and asked the household to help complete it. The questionnaires aimed to assess collective and not individual knowledge. After collection of all the pre and post- test questionnaires, the data were analyzed using appropriate statistical methods. All data were analyzed using the Statistical Package for Social Sciences version 11. Differences before and after intervention were investigated using paired-sample t-test and chi-square test. A p value 0.05 was considered as significant. A total subjects of 1000 fifth grade students were invited of which 701 [394 boys and 307 girls] accepted to participate in the study. There was a significant improvement in the cardiovascular knowledge scores of parents after intervention (p=0.001). We presented the “before and after intervention knowledge levels of parents” in Table 1.

There was a greater rise in the health knowledge scores of sons’ families in comparison to daughters’ families (p=0.004). Educational levels of the families had no significant effect in raising their knowledge after intervention (p=0.28). In addition, no difference was observed between the families with university education and those without university education (p=0.65).

In evaluating the role of nutrition of CAD in pre test, 85% of the families knew about the effect of nutrition on CAD. However, after intervention this rate increased to 92.1%. In asking the subjects on the factors which caused overweight and obesity, 94.8% of the subjects believed that it is caused by overeating and low physical activity. In pre-test, 95.2% believed that regular diet and exercise are the best ways to control body weight. However, after intervention this rate increased to 98.6%. Coronary heart disease is currently the leading cause of mortality and morbidity in Iran. Several risk factors are known to be associated with an increased incidence of cardiovascular disease. These risk factors often have their roots in childhood. As for improving some of the cardiovascular risk factors like sedentary lifestyle and nutrition the entire family must be involved, so primary prevention and intervention through risk factor modification can be effective in both the children and their parents. Most of the school-based health programs are not only directed to children but also to all groups in order to promote healthy lifestyle. The present study is one of the few school-based programs in Iran. Our aim was to increase the knowledge in families of children in order to induce positive health behaviors both in children and their families. To assess the effectiveness of intervention components, we need to increase health knowledge first, so our primary outcomes were to increase knowledge on high-fat foods and other classic risk factors for cardiovascular disease. We used family packs and trigger objects (T-shirts) to motivate the subjects. Based on the results of our studies and regarding the fact that our population is very young, we suggest using school-based programs for promoting healthy lifestyle in the general population. The difference between sons’ and daughters’ families in health knowledge may be due to our cultural background in which families pay more attention to boys in comparison to the girls. One of the limitations of our study was that we did not divide the children into intervention and control groups. The reason was that we needed a strong incentive for children to participate in the study. As the trigger objects were planned to be awarded just to the intervention group, we experienced some problems in allocating children to the control group. For this reason, we could not compare the efficacy of this method with other studies. Ineffectiveness of the role of parental educational on cardiovascular health knowledge suggest that in our country health educational programs are successful in all families regardless of the difference between their educational levels.

This school-based educational intervention program was effective in improving cardiovascular risk factor knowledge in both the children and their families in

<table>
<thead>
<tr>
<th>Knowledge level</th>
<th>Frequency (%)</th>
<th>Sons</th>
<th>Daughters</th>
<th>Sons</th>
<th>Daughters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td></td>
<td>4 (1)</td>
<td>7 (23)</td>
<td>3 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td>139 (35.3)</td>
<td>115 (37.5)</td>
<td>42 (10.9)</td>
<td>54 (18.1)</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td>251 (63.7)</td>
<td>185 (60.3)</td>
<td>340 (88.3)</td>
<td>245 (81.9)</td>
</tr>
</tbody>
</table>
addition to being cost-effective. However, the long-term effects remain to be evaluated. Further studies are warranted to assess the impact of such program on cardiovascular health attitudes and behaviors.

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References


Changes of the immune status in pregnancies complicated by diabetes

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Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defect in the insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs.1 Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy and in most cases resolves after pregnancy. Virtually, all new cases of diabetes in pregnancy are a transient form of type 2 DM. The prevalence of GDM in a given population is thought to vary in direct proportion to that of type 2 DM. This depends on the various demographic characteristics of the specific geographic population, including age and ethnic group, and is generally reported as 2-5%.

Approximately 50% of women diagnosed with GDM during pregnancy develop overt type 2 DM.1 Usually during mammalian pregnancy, large physiological adjustments are required in the mother. These changes result from signals passing between the conceptus (especially the trophoblast) and the mother throughout pregnancy. Immune adaptation is not required for the mother to cope with the fetus as an allograft. The lack of HLA antigens on the syncytiotrophoblast and the presence of only the non-classic HLA G antigen on the cytotrophoblast cells precludes the fetal trophoblast from playing any part in currently recognized types of allogeneic immune reactions. All these reactions depend on the cellular recognition processes associated with the major histocompatibility complex classes I and II, therefore, the maternal immune system fail to be stimulated by allogeneic trophoblast, but allogeneic trophoblast cannot be the target for otherwise armed maternal cytotoxic T cells. Furthermore, according to current understanding of the phenomenon of “major histocompatibility complex restriction,” the absence of classic major histocompatibility complex antigens on the trophoblast will prevent the corecognition of any other form of cell surface antigens that it might express.

So the mother is not “immunodeficient”: but she remains immunocompetent throughout pregnancy.2 This study was conducted on a 40 pregnant ladies in their third trimester of pregnancy who were admitted to the obstetrical ward in Al-Kadhmiya teaching hospital/Baghdad from January 2005 to December 2005 for control of their blood sugar, 20 of them were diagnosed as gestational diabetes in current pregnancy (all of them had impaired glucose tolerance test), another 20 patients included in the study were known diabetic patients before pregnancy in their third trimester of pregnancy. Ten pregnant ladies comparable to the same age and gestational age, without any current or previous medical history for diabetes were taken as control positive group. And 10 non-pregnant ladies comparable to same age were taken as control negative. Cases with multiple pregnancies were excluded from the study. Blood sample (5 milliliters of blood) were collected from each patient without anticoagulant, let to clot and then centrifuge at 3000 rpm for 5 minutes to separate the serum which was stored at -20°C until used. Quantitative measurement of serum immunoglobulin (IgG, IgM, IgA) and complement (C3 and C4) were measured by single radial immuno-diffusion method (Bio meghrab...
Changes of the immune status in pregnancies complicated by diabetes

Table 1 - The concentrations of immunoglobulins (IgG, IgM, IgA) and complements (C3 and C4) in all groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Gestational diabetes mellitus (n=20)</th>
<th>Pregnant diabetics (n=20)</th>
<th>Control groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>P value</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>IgG mg/dl</td>
<td>267 ± 18.8</td>
<td>&lt;0.01</td>
<td>253 ± 16.9</td>
</tr>
<tr>
<td>IgM mg/dl</td>
<td>11.4 ± 1.4</td>
<td>&lt;0.01</td>
<td>10.5 ± 1.7</td>
</tr>
<tr>
<td>IgA mg/dl</td>
<td>225 ± 19.6</td>
<td>&lt;0.01</td>
<td>189 ± 18.8</td>
</tr>
<tr>
<td>C3 mg/dl</td>
<td>23.5 ± 21.6</td>
<td>&lt;0.01</td>
<td>55.12 ± 24.7</td>
</tr>
<tr>
<td>C4 mg/dl</td>
<td>10.5 ± 9.8</td>
<td>&lt;0.01</td>
<td>12.2 ± 2.7</td>
</tr>
</tbody>
</table>

kit). Concentration is determined according to the manufacturer’s protocol. Statistical analysis were carried out using t-test, P value of a level less than 0.05 was considered statistically significant. Level of IgG, IgM and IgA and C3, C4 in the maternal serum were assessed and compared with the control positive and negative group. The serum levels were decreased in cases of diabetes and gestational diabetes also in healthy pregnant mothers it was statistically significant as shown in Table 1. In this study, the humoral immunity (IgG, IgM, IgA) and complements (C3, C4) were found to be decreased in pregnant women and there is further decrease in cases complicated with diabetes when compared to non-pregnant healthy women. It has been observed that the high levels of sex hormones (particularly progesterone) which exist during pregnancy induce a state of immune suppression and specifically humoral immunity. This is logically assumed to be required in order that the pregnant woman not reject the fetus, which, after all, is a “foreign object”. Gestational diabetes and insulin-dependent diabetes are characterized by distinct pathophysiological mechanisms. However, their presence in pregnancy poses similar risks to the fetus. It is possible that factors common to both diseases are responsible for the increased morbidity and mortality in the offspring of such pregnancies. In a study carried out by Galbraith et al on placentae from insulin-dependant diabetics revealed large quantities of complement components C4 and C3 in the intervillous spaces and trophoblast found in placentae from insulin-dependant diabetics, suggesting that glucose tolerance in pregnancy, even of minor degree, is frequently associated with immunopathological processes that are reflected in the placenta. A cross-sectional study carried out by Engstrom et al on diabetic men reported strong correlations between plasma levels of complement C3, insulin and glucose are associated with development of diabetes. Another study concluded that humoral immunity is more deranged in type 2 DM compared with type 1 DM. Probably as a result of hyperinsulinemia associated with insulin resistance, while another studies which is goes with our study, found that different disturbances in humoral innate immunity have been described in diabetic patients (low complement factor-4, decreased cytokine response after stimulation), the maternal immune response may be modulated away from cellular responses towards humoral immunity, not all of which depends on recognition of major histocompatibility complex antigens.

In conclusion normal pregnancy results in a significant change in certain key cells that make up the body’s immune response. These cells prepare the mother to fight off infection, yet protect the growing fetus from being rejected as a foreign invader, diabetes also associated with immune disturbance which is further compromised if it complicate pregnancy wither gestational, type 1 DM or type 2 DM.

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References


A high rate of caesarean section at a newly opened university hospital

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Cesarean delivery is a common obstetric procedure. Approximately one in 4 pregnant women will deliver by cesarean section.1 It is questionable if this high rate is associated with a decreased perinatal mortality rate.2 However, it is certain that cesarean sections are associated with an increased rate of maternal mortality and morbidity.3 The risk factors for having a cesarean section varies. The high incidence of cesarean section has been the cause of intense debate and analysis. While it is generally accepted that the overall incidence of cesarean section is high, it is felt that some cesarean sections are unnecessary.4 A cut down on cesarean sections performed for indications were possible wide inter-observer variation may exist could have a noticeable impact on attempts at reducing the cesarean section rates. The purpose of our study was to determine the statistical status of these variable rates of indications for cesarean section in our population.

We conducted a retrospective review of the hospital obstetric records of all women who had a cesarean delivery between 1st January 2004 and 31st December 2004 at King Abdullah University Hospital (KAUH) of the Jordan University of Science and Technology in Irbid, North Jordan. This is a community-based tertiary referral center with a patient population cared for by public-sector specialist, university teaching staff, physicians, obstetrics and gynecology residents. For the same period a similar review was conducted of all women who had a cesarean delivery at Princess Badea Teaching Hospital (PBTH) in Irbid, North Jordan, a National Health Service maternity hospital open to the general population. It is staffed with public-sector obstetrics and gynecology specialists and residents. Cesarean delivery indications were recorded for all deliveries. When more than one indication was found, a single diagnostic classification was assigned for statistical analysis. Demographics and significant aspects of the obstetric history were recorded. Antepartum obstetric complications were identified, including chronic hypertension, preeclampsia, preterm labor, premature rupture of membranes, preexisting and gestational diabetes, asthma and thyroid disease. Factors that could have an impact on the need for cesarean section were reviewed, which included the use of oxytocin (for either augmentation or induction), epidural anesthesia and amniotomy. Cervical dilatation at the time of primary cesarean delivery was also recorded. Fetal outcome variables were recorded. These included fetal weight and Apgar scores. During the time interval between 1st January 2004 and 31st December 2004, there was a total 1010 deliveries in KAUH. Of whom 368 had cesarean delivery (36.43%). Of these, 146 (39.7%) were elective and 222 (60.3%) were emergency procedures. Of the total number of patients who underwent cesarean section, 58% had booked for their antenatal care and delivery at the hospital, 23.9% were self referrals; the remaining 18.1% were referrals from other hospitals. There were 8362 deliveries at PBTH with a cesarean section rate of 18.32%. Elective cesarean delivery was performed in 22.1% of cases while emergency cesarean section was performed in 77.9% of cases. The leading indication for surgery was 2 or more previous cesarean section (4.24%), followed by fetal distress (2.76%), breech presentation (2%), failure to progress in labor (1.94%) and severe pre-eclamptic toxemia (PET) (1.04%). Sixty-five percent of patients had booked for their antenatal care and deliveries at the hospital, 25% were self referrals; the remaining 10% were referrals from other hospitals. The list of indications and the corresponding number of patients for the 2 hospitals is presented in Table 1. The leading 5 indications for surgery were 2 or more previous cesarean section (6.63% for KAUH and 4.24% for PBTH), followed by fetal distress (5.44% for KAUH and 2.76% for PBTH), breech presentation (3.96% for KAUH and 2% for PBTH), failure to progress in labor (3.46% for KAUH and 1.94% for PBTH) and severe PET (3.46% for KAUH and 1.04% for PBTH). All these indications were statistically significant (p<0.001). Cesarean deliveries occur for a variety of indications; thus, some factors are amenable to intervention strategies for reduction of the overall rate. Patient characteristics and indications leading to cesarean delivery are heterogeneous.5 The

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Reduction strategies of cesarean section rates

**Table 1** - Indications for cesarean section at Princess Badea Teaching Hospital (N=1532 of 8362 deliveries) and King Abdullah University Hospital (N=368 of 1010 deliveries).

<table>
<thead>
<tr>
<th>Indication</th>
<th>PBTH (N = 8362)</th>
<th></th>
<th>KAUH (N = 1010)</th>
<th></th>
<th>Odds ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous 2 or more CS</td>
<td>355 (4.24)</td>
<td>67 (6.63)</td>
<td>67 (6.63)</td>
<td>0.62</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Fetal distress</td>
<td>231 (2.76)</td>
<td>55 (5.44)</td>
<td>55 (5.44)</td>
<td>0.42</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Breech presentation</td>
<td>168 (2)</td>
<td>40 (3.96)</td>
<td>40 (3.96)</td>
<td>0.5</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Failure to progress</td>
<td>163 (1.94)</td>
<td>35 (3.46)</td>
<td>35 (3.46)</td>
<td>0.55</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Severe pre-eclampsia</td>
<td>87 (1.04)</td>
<td>35 (3.46)</td>
<td>35 (3.46)</td>
<td>0.29</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Multiple pregnancy</td>
<td>60 (0.71)</td>
<td>22 (2.17)</td>
<td>22 (2.17)</td>
<td>0.32</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Unstable or abnormal lie</td>
<td>39 (0.46)</td>
<td>22 (2.17)</td>
<td>22 (2.17)</td>
<td>0.21</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Ante-partum hemorrhage</td>
<td>57 (0.68)</td>
<td>19 (1.88)</td>
<td>19 (1.88)</td>
<td>0.36</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Previous CS and others</td>
<td>151 (1.8)</td>
<td>15 (1.48)</td>
<td>15 (1.48)</td>
<td>1.22</td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>Infertility</td>
<td>58 (0.69)</td>
<td>12 (1.18)</td>
<td>12 (1.18)</td>
<td>0.58</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Bad obstetrics history</td>
<td>6 (0.07)</td>
<td>6 (0.59)</td>
<td>6 (0.59)</td>
<td>0.12</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Failed induction of labor</td>
<td>79 (0.94)</td>
<td>6 (0.59)</td>
<td>6 (0.59)</td>
<td>1.60</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td>Intra-uterine growth restriction</td>
<td>6 (0.07)</td>
<td>5 (0.49)</td>
<td>5 (0.49)</td>
<td>0.14</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Tubal ligation</td>
<td>8 (0.09)</td>
<td>5 (0.49)</td>
<td>5 (0.49)</td>
<td>0.19</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Cephalopelvic disproportion</td>
<td>5 (0.05)</td>
<td>4 (0.39)</td>
<td>4 (0.39)</td>
<td>0.15</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Macrosomia</td>
<td>15 (0.17)</td>
<td>3 (0.29)</td>
<td>3 (0.29)</td>
<td>0.6</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>1 (0.01)</td>
<td>2 (0.19)</td>
<td>2 (0.19)</td>
<td>0.06</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Cord prolapse</td>
<td>20 (0.23)</td>
<td>2 (0.19)</td>
<td>2 (0.19)</td>
<td>1.21</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>Medical problems</td>
<td>6 (0.07)</td>
<td>2 (0.19)</td>
<td>2 (0.19)</td>
<td>0.36</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>Pelvic floor repair</td>
<td>4 (0.04)</td>
<td>2 (0.19)</td>
<td>2 (0.19)</td>
<td>0.24</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Cervical fibroid</td>
<td>3 (0.03)</td>
<td>1 (0.09)</td>
<td>1 (0.09)</td>
<td>0.36</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>10 (0.11)</td>
<td>8 (0.79)</td>
<td>8 (0.79)</td>
<td>0.15</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1532 (18.32)</td>
<td>368 (36.43)</td>
<td>368 (36.43)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PBTH - Princess Badea Teaching Hospital, KAUH - King Abdullah University Hospital, CS - cesarean section

Relative contributions of various indications does vary and may be related to the status of the population of a particular hospital, the referral pattern and the interpractitioner variability in practice implementation. Strategies to reduce cesarean delivery rates must address these differences.

Our finding that 39.7% of cesarean deliveries were elective procedures represents a sizable contribution that might be amenable to intervention strategies. If all patients in the elective cesarean section group for indications other than 2 or more previous cesarean sections had been given a trial of labor, this would have decreased the overall cesarean section rate. If the 79 patients in this group had a 75% success rate similar to that reported in other studies, 4,5 59 cesarean sections would have potentially been eliminated and the cesarean delivery rate would have been decreased to 30.6% from 36.43%, approximately a 16% reduction. The emergency cesarean sections represented 60.3% of cases. A leading indication in this category was fetal distress (5.4%). This has been responsible for most of the increase in cesarean section rate in other hospitals. 4 The finding that one-third of all the cesarean sections carried out for fetal distress were thought to be unnecessary or premature confirms an over diagnosis of this condition. 4 Fetal heart rate monitoring lacks specificity. 6 It has been recommended that fetal pH assessments should be conducted instead of immediate cesarean section. 4 If a third of fetal distress cases have been unnecessary, then the total expected reduction in our cesarean section rate would be almost 5% of the overall cesarean section rate. This rate of reduction would be a worthwhile objective, especially if this reduction could be achieved without an increase in the risk to the fetus. The percentage of our
patients experiencing a trial of labor was not analyzed. A rate of approximately 70% has been reported with
a success rate of approximately 75% of vaginal birth
after cesarean. This is a likely scenario if trials of labor are
characterized by less frequent inductions of labor, more
use of amniotomy, late epidural placement, and
less repeat cesarean for dystocia performed in the latent
phase of labor. A reduction in the primary cesarean
section rate would lead to a reduction in that of the
repeat cesarean section. Analysis of multicenter statistics
has found that approximately 35% of cesarean sections
were repeat procedures. Thus, reductions in the number
of repeat cesarean deliveries would be expected to lower
the overall cesarean delivery rate significantly. It has
been estimated that if 80% of patients with a previous
cesarean delivery attempted a trial of labor, an overall
success rate of 75% would lead to a 21% reduction in
the national cesarean delivery rate.

In conclusion, the relative rates of indications for
cesarean sections are heterogeneous; thus, some are
amenable to overall rate reduction strategies. The
combination of fewer women undergoing cesarean
section for fetal distress and more women experiencing
external cephalic version and a trial of labor and the
enforcement of more strict criteria for the diagnosis of
dystocia would result in more patients achieving a
vaginal delivery.

Acknowledgment. We are grateful to Dr. S. Howari, Dr. D. Suhail,
Dr. A. Edwan, Dr. R. Obeidat, Dr. H. Rawashdeh and Dr. R. Kharabsheh for
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administrative data to identify indications for elective primary
cesarean delivery versus trial of labor: a prospective multicenter

Loss of zonal organization of articular cartilage after experimental subchondral trauma of the knee joint

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Harry Merk, PhD.

The healthy articular cartilage shows a superficial, a
transition, a deep radial, and a deep calcified
zone, which in light microscopic findings can be
distinguished, especially by Safranin-O-Staining
representing the proteoglycan content. The commonly
used histopathological grading systems show a lack of
validity especially in the scoring of mild to moderate
cartilage damage, and the physiological zonal formation
is mainly not a parameter for the quality of the
cartilage. Intra- and inter-observer reproducibility in
these systems are not satisfying in the grading of
osteoarthritis. In several studies, models have been
described for the Photoshop-based image analysis for
the quantification of proliferative activity and of
hormone receptor expression in invasive breast cancer.
Meanwhile, Photoshop-based image analysis has been
used in different kinds of analysis of cartilage and bone
samples, and also to demonstrate the medium term
influence of subchondral damage on the articular
cartilage, measured by Safranin-O for proteoglycans
and by Alcian blue for glycosaminoglycans. Other
possible options are PAS for glycoproteins and
immunostaining, for example, collagen I and II. It can
replace subjective evaluations of color intensities, but it
is not meant as another grading system, and it should
and cannot contain a classification of arthritis. The
benefit of quantifying changes in articular cartilage is
well established in animal models, as more attention is
paid to the description of biomechanical factors of the
subchondral bone leading to cartilage damage. Meanwhile,
many studies have shown that MRI can
accurately and non invasively evaluate post traumatic
changes defined as bone bruises, sub and osteochondral
fractures, and even provide information about the

stability of the lesion, as microfractures of bone trabeculae might lead to inadequate mechanical support of the subchondral plate and subsequent overloading of the cartilage itself. In clinical and experimental studies, the histopathological and cryosectional appearance of the lesions could be identified as microfractures of cancellous bone and weight-bearing trabeculae, edema, and bleeding of fatty marrow. The purpose of the present study is to demonstrate meaningful reproducible image analysis of different kinds of staining concerning the above mentioned zonal formation and its loss in post trauma cartilage changes can be performed using inexpensive widely distributed graphics software (Adobe Photoshop). After staining, this technique is fully computerized without any manual interference at any step and is very reliable for the objective quantification of any pattern of osteoarthritis and assessing especially the loss of zonal formation. The present study was performed in the University Hospital Freiburg, Germany from June 2001 to July 2002. In a previous study, an experimental animal model was introduced to produce pure subchondral damage without affections to the articular cartilage. In a preliminary cadaver test and later in a main study with living beagle dogs, reproducibility of the transmitted forces under identical conditions could be shown. In the present subsequent study in 12 adult beagle dogs, the medium term effect of a pure subchondral fracture of the lateral aspect of the trochlea on the initial healthy cartilage was examined. The study was performed in accordance with the German law for animal protection and had been approved by the Review Board for the Care of Animal Subjects at the Regierungspräsidium, Freiburg, Germany. The non-impacted left knee was examined as a control knee in every animal. The transarticular force is maintained via patella to the lateral aspect of the trochlea by a weight that is dropped onto the patella of a rigidly held knee joint of an anesthetized dog. The construction consists of a drop-tower, a drop weight of 2.1 kg with a force transmitting rod-tip with a diameter of 1.9 cm (adapted to the dog’s patella), a load cell (Kistler, Swiss Type 5001) and a force transducer (Kistler, Quarz). The transmitted forces are recorded on an oscilloscope with settings of 0.5 msec/div. and 0.5 V/VDN (1V/1000 N). After the animal was anesthetized it lies in lateral recumbency with the hip abducted and 90 degrees flexed. The tibia is held in 100 degrees of flexion in the knee joint, the whole lower extremity is secured rigidly with the thigh positioned in a frame. Radiographs in sagittal and axial views in pre-impact state were performed for a correct perpendicular impact. The force is induced by the fall of the released weight over a prescribed distance. General anesthesia was induced with 0.3 mg/kg Midazolam (Dormicum), intravenous (IV), followed by 5-6 mg/kg Propofol (Disoprivan), IV and after endotracheal intubation, maintained by the IV infusion of 0.3 mg/min Propofol and repeated IV bolus of 0.05 mg/kg Fentanyl (Fentanyl-Janssen). At the end of anesthesia, and for the next 3 days they received Caprofen (Rimadyr) subcutaneously 4 mg/kg once daily to achieve post-operative analgesia. Both knee joints were examined by MRI using a 1.5 Tesla imaging unit (Vision, Siemens, Erlangen, Germany) using a head coil and a small surface ring coil. The first MRI examination was 4 hours after impact and consisted of, besides the standard T1 and T2 weighted sequences, Fast T1-weighted (Spin Echo) SE-sequences (TR/TE 550/14 ms) in 3 perpendicular planes, T1-weighted SE sequences (TR/TE 420-535/12-17 ms) with slice thickness 3 mm and a 240 x 256 matrix (sagittal), TSE (Turbo Spin Echo) with spectral fat saturation T2-weighted (Turbo factor = 15, TR/TE 2900/120 msec), slice thickness 3 mm (sagittal), fat suppressed TIRM-sequences (Turbo Inversion Recovery Magnitude) with slice thickness 4 mm, TR/TE 6194/60 msec (sagittal) and 3D FLASH, (fast-low angle shot) fat-suppressed sequences, TR/TE 48/11 msec. Flip angle = 40°, 336 x 512 matrix, slice thickness 1.5 - 2 mm (sagittal). As described before, on follow-up 6 months after producing a subchondral fracture in each dog, osteochondral sections were taken from both the area above the former subchondral lesion (serial sections in cases without visible cartilage damage) and the corresponding area of the non-affected knee joint. After fixation and decalcification in ethylenediamine tetraacetatic acid (EDTA), the sections were fixed, decalcified in EDTA, dehydrated, and embedded in paraffin (5 µm slice thickness). Hematoxylin-Eosin, van Gieson, Safranin-O, PAS and Alcian-blue staining was performed using standard methods. It is important to expose the tissues to fix, decalciify, embed, and stain the samples simultaneously, using the same materials.
by one person to decrease non-specific staining. Conventional microscopic pictures were photographed using Axioskop (Zeiss, Oberkochen, Germany) with 10x optics and Kodak Elite 400. Using Adobe Photoshop, the digitized images (x50) of the Safranin-O and Alcian-blue stains were stored on an external data storage device. Firstly, it was evaluated how large a window was necessary for the accurate determination of coloring per pixel. Using the Magic wand tool in the select similar menu the cursor was placed on the darkest area, because the pixels thus chosen represent the “purest” narrowest color limitation, namely, the smallest variation from the selected color hue and color saturation. Subsequently, every image is transformed to a gray-scale and the total pixel number is determined. The area occupied by any specific color range can be specified and compared in a relative manner directly from the histogram. An optical density plot of the selected area was generated using the histogram tool in the Image grow menu and the mean staining intensity (in arbitrary unit, AU) was recorded. When the Histogram menu is selected, a display appears depicting gray levels (black/white) or luminosity (color) of all pixels within the selected area, including mean, median, and standard deviation, pixels, and so forth. Standard deviation of the images expresses the variability of the coloring and especially, in case of articular cartilage, the decrease in typical zonal formation in the analysis of hyaline cartilage. Statistical analysis was performed using the t-test. After producing the acute subchondral fracture the intact articular cartilage was demonstrated in the FLASH 3D®-sequences in all 12 affected knees with a comparison of the healthy control knee. The subchondral fractures (microfractures) with bleeding are shown by a decrease of signal intensity on TIRM and T1-weighted images due to a transformation of hemoglobin to deoxyhemoglobin or even methemoglobin. The comparability of these MRI-detected lesions with microfractures of the cancellous bone has been demonstrated in our previous study. In no case was any intra-articular structure affected by impact. In the safranin-O-stains, we found a decrease in standard deviation of the pixel analysis in 11 of 12 cases, 9 of them with a large amount of more than 10% showing a uniform staining in the different zones compared with the healthy cartilage. Exceptions were dogs 4 and 9 with no relevant differences in cartilage degeneration, and dog 8, which showed extended scar tissue leading to a large intensity difference compared with the surrounding tissue, and an increase in standard deviation. In general, decreases in standard deviation were less severe in those stains with scar tissue formation, as these areas show different signal intensities compared with “normal tissue.” The results of the measurement of standard deviation of Alcian-blue-staining revealed slightly smaller decreases of the standard deviation in the most of the 12 dogs with very small differences in dogs 4, 9, and 11. Diagrams in the Image menu reveal mean, standard deviation, and other statistical parameters for t-test (Figure 1). A p-value less than 0.001 was reached for Safranin-O-staining and Alcian Blue staining. Different kinds of cartilage and matrix components have already been analyzed using Adobe Photoshop. It has become a valuable supplement for well known histopathological grading systems of articular cartilage damage. Years before, the method had already become an accepted tool in the quantification of immunocytochemical hormone receptor studies in oncology and neuropathology and a very good correlation has been found between Photoshop based image analysis and biochemical techniques, for example, enzyme immunoassay. However, although these approaches are suitable for comparative assessments, quantification of the absolute amount of proteoglycan, glycoproteins, or other molecules is not allowed, as the area occupied by one particular color range can be specified and compared in a relative manner. In our experiment, Photoshop-based image analysis has been used to demonstrate the medium term influence of subchondral damage on the classical zonal formation of articular cartilage, measured by Safranin O for proteoglycans in the specific zones, and is not so good with Alcian blue as it represents the amount the polysaccharide components of the proteoglycans. Other possible options are PAS for glycoproteins and immunostaining. Histology and biochemical analysis of cartilage shows that chondrocytes from the various zones differ in several parameters, for example, in matrix synthesis. The PAS staining reveals good comparisons of the total amount of staining but has a limited applicability for deviations in the different cartilage layers. In several studies, follow-up MRI or arthroscopy some months after subchondral damage has shown alterations of the hyaline articular cartilage, which had not revealed any evidence of damage during the initial examination. Johnson et al reported an increased loss of joint homeostasis in patients who had sustained subchondral damage in addition to an anterior cruciate ligament (ACL) injury as well as a higher complication rate in such patients after ACL-reconstruction. Unfortunately, many times, subchondral edema, subchondral fracture, and even osteochondral fractures are not clearly distinguished. Therefore, Miller et al found complete resolution of subchondral signal changes in their repeat MRI of patients with former isolated medial collateral ligament injury. The groups that correlated MRI with histological findings could distinguish lesions as...
Loss of zonal organisation of articular cartilage

3. Miller MD, Osborne JR, Gordon WT, Hinkin DT, Brinker

References


Beneficial effects of soy protein isoflavones on lipid and blood glucose concentrations in type 2 diabetic subjects

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Hosain M. Haghighizadeh, PhD.

Evidence is emerging that dietary supplementation with soyprotein have a beneficial role in type 2 diabetes.1,2 Nutritional intervention studies performed in animals and humans suggest that the ingestion of soyprotein with isoflavones and flaxseed rich in lignans improves glucose control and insulin resistance.3 In animal models of obesity and diabetes, soyprotein has been shown to reduce serum insulin and insulin resistance.2 In studies of human subjects with or without diabetes soyprotein also appears to improve hyperglycemia and reduce body weight, hyperlipidemia and hyperinsulinemia and supporting its beneficial effects on obesity and diabetes.1,2

A meta-analysis of 38 controlled clinical trials indicated that soyprotein was effective in lowering plasma cholesterol, low density lipoprotein (LDL) cholesterol, and triglycerides (Tg) concentration.4 The purpose of the present study was to assess the effects of a processed defeated meal containing soyprotein 98 gr/100 gr and isoflavones 195 mg/100 gr taken one time daily as a beverage with regular meals for 3 months, on serum levels of total cholesterol, Tg, high density lipoprotein (HDL), LDL, fasting blood sugar (FBS), glycosylated hemoglobin weight and blood pressure.

Twenty-six type 2 diabetic subjects who were referred to Ahvaz Jondishapur University, diabetes center for uncontrolled diabetes, completed the study. Eleven patients had previous history of hypertension and 3 of microalbuminuria. All of the patients were treated with diet and anti diabetic drugs (18 sulfonylureas, 11 metformin, 4 combined sulfonylureas and metformin and 1 insulin). They took the prescribed medicine throughout the study without any changes. Subjects were asked to maintain their habitual diet and level of physical activity throughout the study. All were in good general health and had a normal renal function. Informed written consent was obtained from each subject. All subjects received 25 gr/day defeated soyprotein meal providing a daily amount of 12 gr soyprotein with 50 mg isoflavones for 3 months. Subjects were instructed to mix their daily supplement in 200 ml water and consume as a beverage with their current meals. The participants were weighed monthly. Blood samples for measuring FBS, HbA1C, total cholesterol, Tg and HDL-cholesterol were obtained after an overnight fasting period before the study and monthly thereafter. The LDL cholesterol was calculated using the Friedwald equation. Blood pressure was measured before the study and at each monthly visit. Plasma glucose concentrations were measured by the glucose oxidase method and HbA1C by high performance liquid chromatography Serum Tg, total cholesterol and HDL-cholesterol were measured by pars Azemon kits on a RA-XY and RA-1000 Automatic Analyzer ( Pars Azemon Company, Tehran, Iran). Statistical analysis was performed using the Statistical Package for Social Sciences version 11.5. Significant point was set at 0.05 level. A total of 26 (17 female and 9 male) type 2
Table 1 - Blood glucose, lipids and blood pressure before, during and after 3 months consumption of soy product.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before study</th>
<th>After 1 months</th>
<th>After 2 months</th>
<th>After 3 months</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS (mg/dl)</td>
<td>178 ± 60</td>
<td>16 ± 63</td>
<td>157 ± 53</td>
<td>152 ± 50</td>
<td>0.015</td>
</tr>
<tr>
<td>Glycosylated hemoglobin %</td>
<td>9.6 ± 1.7</td>
<td>9.3 ± 1.5</td>
<td>9 ± 1.3</td>
<td>8.8 ± 1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>114 ± 38</td>
<td>112 ± 35</td>
<td>114 ± 38</td>
<td>110 ± 37</td>
<td>0.076</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>46 ± 6</td>
<td>44 ± 6</td>
<td>45 ± 5</td>
<td>45 ± 5</td>
<td>0.27</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>267 ± 149</td>
<td>261 ± 146</td>
<td>243 ± 122</td>
<td>229 ± 113</td>
<td>0.008</td>
</tr>
<tr>
<td>Chol (mg/dl)</td>
<td>207 ± 42</td>
<td>203 ± 40</td>
<td>203 ± 40</td>
<td>196 ± 41</td>
<td>0.002</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>138 ± 31</td>
<td>132 ± 23</td>
<td>131 ± 18</td>
<td>130 ± 21</td>
<td>0.101</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>87 ± 20</td>
<td>84 ± 16</td>
<td>84 ± 15</td>
<td>84 ± 16</td>
<td>0.384</td>
</tr>
</tbody>
</table>

FBS - fasting blood sugar, LDL - low density lipoprotein, HDL - high density lipoprotein, TG - triglyceride, Chol - cholesterol, BP - blood pressure

Beneficial effects of soy protein isoflavones

diabetic patients completed the study. Soy preparation was well tolerated. Patients age were between 39-70 years (54 ± 8.4 years). Mean time from diagnosis of type 2 diabetes was 6.5 ± 4.3 years (between one month to 15 years). The FBS and HbA1C levels decreased significantly after 3 months consumption of this soy product (152 ± 50 versus 178 ± 60 and 8.8 ± 1.4 versus 9.6 ± 1.7 percent respectively). Although serum total cholesterol (p<0.002) and Tg (p<0.008) levels lowered significantly after 3 months, there were no significant differences in LDL and HDL cholesterol levels (Table 1). Systolic and diastolic blood pressure and patients weights remained unchanged during the study. Only FBS level showed significant changes in first (p<0.03) and second (p<0.02) months after consumption of soy product. The soyprotein isoflavones (SPI) used in this study reduced FBS by 15%, HbA1C by 7%, TG by 14% and total cholesterol concentrations by 5%. The results showed that soy supplementation has a significant effect on both glycemic control and lipid profile in type 2 diabetes patients. The therapeutic potential of soy for diabetes was first suggested in 1910. Few studies of the effect of soy on glycemic control in diabetes have shown inconsistent results that have been primarily attributed to the soluble fiber content of soy bean preparation. In a study of 14 women and 6 men, 6 weeks of treatment with soyprotein (50 gr/day), isoflavones (165 mg/day), and cotyledon fiber (20 gr/day) compared with placebo (case in 50 gr/day and cellulose 20 gr/day) showed an improvement in lipid parameters but no difference in glucose, insulin, or HbA1C. A cross-over trial of soy phytoestrogen (soyprotein 30 gr/day, isoflavones 132 mg/day versus placebo) intake in 32 postmenopausal women with type 2 diabetes for 2 weeks (with a 2 weeks washout period) showed a significant decrease in insulin resistance, HbA1C, total cholesterol, LDL cholesterol and cholesterol/HDL ratio, but no significant changes in HDL cholesterol, Tg, weight and blood pressure. In this study, similar results were obtained regarding fasting blood glucose, HbA1C, total cholesterol, LDL-cholesterol, blood pressure and weight, however, LDL-cholesterol showed no significant decrease. In vitro studies suggested several mechanisms for a direct pharmacological action of soy on glycemic control, including a tyrosine kinase inhibitory action, changes in insulin receptor numbers and affinity, intracellular phosphorylation and alterations in glucose transport. 

In this study, decreases in both FBS and HbA1C without any changes in patient’s weight seems to support a direct favorable effect of soy in these patients. The mechanisms for the lipid lowering effect of soy products are not known. There is persuasive evidence to implicate soy protein in the cholesterol-lowering effect. Soyprotein provide a large amount of protein with high-quality amino acids, which seems to upregulate LDL receptors directly by 50% or more. The meta analysis of Anderson et al however, indicated that a considerable proportion of the effect of soy products on serum cholesterol might be linked to the effects of isoflavones. Since isoflavones are compounds that have structure similar to estrogens and bind to estrogen receptors, it has been postulated that this may be responsible for the effects of soyprotein on serum lipids.
In conclusion, these results indicate beneficial effects of dietary supplementation with soy product on blood glucose and lipid profile of these type 2 diabetic patients. Thus, a dietary supplementation with soy protein isoflavones in type 2 diabetic patients may provide an acceptable and effective option for blood glucose and lipid control, thereby decreasing the requirement for drug therapy in these patients.

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References


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