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**Examples**:

- Nishimura (2000), Agindotan et al. (2003), (Kelebeni, 1983), (Usman and Smith, 2001), (Chege, 1998; Stein, 1987a,b; Tijani, 1993,1995), (Kumasi et al., 2001)

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The Introduction should provide a clear statement of the problem, the relevant literature on the subject, and the proposed approach or solution. It should be understandable to colleagues from a broad range of scientific disciplines. The presentation of the case study should include the important information regarding the case. This must include the medical history, demographics, symptoms, tests etc. Kindly note that all information that will lead to the identification of the particular patient(s) must be excluded.

The conclusion should highlight the contribution of the study and its relevance in general medical knowledge.

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References: Same as in regular articles.

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A review of the types of presentation among positive angiographic acute coronary syndrome patients in Hospital Universiti Sains Malaysia

Nasir Mohamad¹, Norhaya Abdullah¹, Zurkurnai Yusuf², Chew Ken Sheng¹, Nor Hidayah Abu Bakar³, Ilya Irinaz Idrus¹, Rashidi Ahmad¹, Nik Hisamuddin Nik Abdul Rahman¹

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Accepted 24 January, 2012

Atypical presentation of myocardial infarction is recognized as an important manifestation of coronary heart disease associated with unfavorable prognosis. Understanding the spectrum of clinical symptoms and presentations are essential to diagnose and deliver appropriate rapid treatment to patients in the emergency department. Hence, this study was carried out to identify the type of presentation of acute coronary syndrome (ACS) and its association with the risk factors related to the atypical presentation in population of study. Out of 260 patients, 25.8% had atypical presentation of ACS with the presentation of right sided chest pain (1.8%), burning chest pain (20.9%) and pricking chest pain (15%). The significant associated diseases were diabetes mellitus and past medical history of ischaemic heart disease (p<0.01) respectively. Other significant associated symptoms were epigastric pain (p<0.001), cough (p<0.01) and giddiness (p<0.01). As a conclusion, ACS with atypical presentations remains an important presentation in the Emergency Department. Despite the availability of advanced medical technology, a thorough history taking remains an important component of diagnosis for a better management and outcome of ACS.

Keywords: Atypical myocardial infarction, common presentation, emergency department.

INTRODUCTION

Despite recent major advances, ACS still pose great challenges to emergency physicians from its diagnostic, therapeutic, and prognostic standpoint. This is partly due to its considerable varied clinical manifestations. For example, the silent or atypical presentations, such as pleuritic or indigestion-like chest pain are recognized as important manifestations of ACS, as most studies suggest that they are associated with unfavorable prognosis (Sigurdsson et al., 1995; Madias et al., 1995). Such atypical presentations are more common among woman and elderly patients (Jayes et al., 1992). Several studies have concluded that between 2 to 8% of all patients with ACS are discharged home from emergency departments (Chris et al., 2001). Unfortunately, a large proportion of these patients sent home with ACS were younger patients presented with atypical symptoms or those who had non-diagnostic electrocardiography (McCarty et al., 1993). This study was carried out to determine the types of presentation of ACS in our patient

Abbreviations: ACS, Acute coronary syndrome; HUSM, Hospital Universiti Sains Malaysia; ICL, invasive cardiac laboratory; SPSS®, social science and statistical package.
population in emergency department as well as the risk factors associated with such presentations.

**METHODOLOGY**

This is a retrospective, a one year cross-sectional study which looked into the types of ACS cases presented to Hospital Universiti Sains Malaysia. Patients with age less than 18 years old and those with pre-existing cardiovascular diseases such as congenital heart diseases and those with underlying valvular diseases were excluded from this analysis even if they have positive angiographic findings. Other than that, all patients with positive angiographic findings were included for the analysis.

We obtained the medical records for angiogram findings from the invasive cardiac laboratory (ICL), HUSM. Data entry, interpretation and statistical analysis were done using the Social Science and Statistical Package (SPSS®) version 12.0. Statistical analysis using the Chi-Square test, Fisher’s exact test and binary logistic regression were employed. Ethical approval for this study was obtained from our institutional ethical review board.

**RESULTS**

A total of 362 patients had coronary angiogram done at ICL, HUSM from 1st January to 31st December 2004. Out of these 362 patients, 285 (78.7%) were enrolled into the study, and 25 were excluded. Among the 285 patients enrolled in the study, 193 (74.2%) had typical presentation and 67 (25.8%) had atypical presentation.

The demographic data of patients presented with acute coronary syndrome revealed no significant statistical difference in the type of presentation between gender, race and age. However, there was a higher numbers of atypical presentation in female, Indian and elderly (Table 1).

Majority of the atypical presentation of ACS are “no chest pain” (35%), “pricking chest pain” (15%) and “burning type of chest pain” (14%). In terms of associated symptoms, significantly more patients present with coughing (9% versus 1%), giddiness (26.9% versus 9.3%) and epigastric pain (31.3% versus 13.0%) in the atypical presentation group versus the typical presentation group (Table 2).

There is also significantly higher percentage of patients with associated diabetes mellitus in the atypical presentation group compared to the typical presentation group (p=0.01) (Table 3). On the contrary, the percentage of patients with associated past history of ischaemic heart disease is significantly higher among the typical presentation group versus atypical presentation group (p=0.01) (Table 3).

**DISCUSSION**

In this study, atypical presentation of ACS constituted 25.8% (67) of patients, which was almost similar to other finding which found 25 to 30% of patients with myocardial infarction were clinically unrecognized because of the atypical presentation, for which they did not seek treatment (Sigurdsson, 1995; Loria, 2008). From our study, women, elderly and Indian had higher atypical presentations, although the result was not statistically significant, as it was limited to the inequality of subjects recruitment. In fact, similar to our findings, other study also found that a woman was more likely to have atypical symptoms compared to men (Roger et al., 2000).

As documented, women with the age of more than 65 years were at higher risk for atypical presentations, which primarily consisted of shortness of breath and epigastric pain (Lusiani et al., 1994). The symptoms of dyspnoea in the setting of myocardial ischaemia may result from the acute loss of myocardial compliance, elevation in left ventricular pressures, and subsequent symptoms of heart failure to present with nausea, vomiting and shortness of breath (Golberg et al., 1998). Those women were more likely to have diabetes mellitus at the time they first experience myocardial infarction compared to men and this might be the reason of why they presented with atypical symptoms (Zucker et al., 1997).

Furthermore, women were more likely to have normal or mild disease and less likely to have left-main and three-vessel disease and were more frequently presented with jaw pain and nausea (Dey et al., 2009). Another possibility was women had difficulty in interpreting the severity of the symptoms. This is further complicated by the confusion that arises when interpreting the perception of the symptoms that they had (Rosenfield et al., 2001). Women are also less likely to be correctly assesses their symptoms (Healy et al., 1991). Atypical symptoms in women may also be mistaken as musculoskeletal, gastrointestinal or neurological in origin and inconsistent

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**Table 1. Demographic data of patients presented with acute coronary syndrome.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Typical</th>
<th>Atypical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Male</td>
<td>155</td>
<td>75.6</td>
</tr>
<tr>
<td>Female</td>
<td>38</td>
<td>69.1</td>
</tr>
<tr>
<td>Racial</td>
<td>179</td>
<td>73.7</td>
</tr>
<tr>
<td>Malay</td>
<td>11</td>
<td>84.6</td>
</tr>
<tr>
<td>Chinese</td>
<td>2</td>
<td>66.7</td>
</tr>
<tr>
<td>Indian</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40</td>
<td>17</td>
<td>89.5</td>
</tr>
<tr>
<td>41-50</td>
<td>44</td>
<td>73.3</td>
</tr>
<tr>
<td>51-60</td>
<td>77</td>
<td>75.5</td>
</tr>
<tr>
<td>&gt;60</td>
<td>55</td>
<td>70</td>
</tr>
</tbody>
</table>

---
Table 2. Nature of chest pain in typical and atypical ACS.

<table>
<thead>
<tr>
<th>Description</th>
<th>Typical</th>
<th></th>
<th>Atypical</th>
<th></th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>193</td>
<td>100</td>
<td>31</td>
<td>46.2</td>
<td>0.01</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>0</td>
<td>36</td>
<td>53.7</td>
<td></td>
</tr>
<tr>
<td>Left Sided</td>
<td>192</td>
<td>99.4</td>
<td>28</td>
<td>37.3</td>
<td></td>
</tr>
<tr>
<td>Right Sided</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>5.9</td>
<td></td>
</tr>
<tr>
<td>Nature</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burning</td>
<td>0</td>
<td>0</td>
<td>14</td>
<td>20.9</td>
<td></td>
</tr>
<tr>
<td>Discomfort</td>
<td>48</td>
<td>24.8</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Heavy</td>
<td>71</td>
<td>36.7</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Pressing</td>
<td>59</td>
<td>30.5</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pricking</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>22.3</td>
<td></td>
</tr>
<tr>
<td>Tight</td>
<td>15</td>
<td>7.7</td>
<td>1</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>0</td>
<td>0</td>
<td>35</td>
<td>52.2</td>
<td></td>
</tr>
<tr>
<td>Radiation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left arm</td>
<td>45</td>
<td>23.3</td>
<td>9</td>
<td>13.4</td>
<td></td>
</tr>
<tr>
<td>Back</td>
<td>8</td>
<td>4.1</td>
<td>3</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>Jaw</td>
<td>20</td>
<td>10.3</td>
<td>4</td>
<td>5.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Lower limb</td>
<td>3</td>
<td>1.5</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Right arm</td>
<td>1</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>116</td>
<td>60.1</td>
<td>51</td>
<td>76.1</td>
<td></td>
</tr>
<tr>
<td>Associated symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palpitations</td>
<td>47</td>
<td>24.4</td>
<td>14</td>
<td>20.9</td>
<td>0.56</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>97</td>
<td>50.3</td>
<td>39</td>
<td>58.2</td>
<td>0.26</td>
</tr>
<tr>
<td>Nausea</td>
<td>32</td>
<td>16.6</td>
<td>8</td>
<td>11.9</td>
<td>0.36</td>
</tr>
<tr>
<td>Vomiting</td>
<td>19</td>
<td>9.8</td>
<td>9</td>
<td>13.4</td>
<td>0.41</td>
</tr>
<tr>
<td>Sweating</td>
<td>65</td>
<td>33.7</td>
<td>16</td>
<td>23.9</td>
<td>0.13</td>
</tr>
<tr>
<td>Syncope</td>
<td>3</td>
<td>1.6</td>
<td>3</td>
<td>4.5</td>
<td>0.17</td>
</tr>
<tr>
<td>Insomnia</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1.5</td>
<td>0.08</td>
</tr>
<tr>
<td>Cough</td>
<td>2</td>
<td>1.0</td>
<td>6</td>
<td>9.0</td>
<td>0.01</td>
</tr>
<tr>
<td>Fever</td>
<td>2</td>
<td>1.0</td>
<td>2</td>
<td>3.0</td>
<td>0.26</td>
</tr>
<tr>
<td>Giddiness</td>
<td>18</td>
<td>9.3</td>
<td>18</td>
<td>26.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>25</td>
<td>13.0</td>
<td>21</td>
<td>31.3</td>
<td>0.01</td>
</tr>
</tbody>
</table>

with the onset of myocardial infarction (Mliner et al., 1999). To overcome these problems in primary care setting especially in emergency department, a range of symptoms presentation in women with myocardial infarction and understanding the disease process in women are very useful (Zbierajewski–Eischeid and Loeb, 2009).

Increasing age was associated with higher chances of getting atypical presentation16. For elderly, it was estimated that only 38% of patients older than 60 years with autopsy proved myocardial infarction, had the correct diagnosis before death (Bayer et al., 1986; Cocchi et al., 1998). Varying factors were thought to contribute to these findings, including decline in mental functions, alteration or absence of pain perception secondary to sensory neuropathies or an altered pain threshold. Impaired communication, difficulty in expressing symptoms and delay in the perception of angina pain also further contributed to the atypical presentation (Ambeptiya et al., 1994). Other than that, the cardiac pain was frequently confused by many co-morbid conditions present in elderly (Gregoratos, 2001). Since the most common atypical presentation of myocardial infarction in elderly was shortness of breath instead of chest pain, this caused difficulty in making a diagnosis (Woon and Lim, 2003; Everts et al., 1996). The presentation of acute
Table 3. The result of associated risk factors with ACS presentations.

<table>
<thead>
<tr>
<th>Risk</th>
<th>Typical</th>
<th>Atypical</th>
<th>Chi-square test (p value)</th>
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myocardial infarction is modified by age-related changes in endothelial function, smooth muscle cell activity, diastolic function and response to circulating catecholamine and these explained why elderly has higher atypical presentation of myocardial infarction (Maheshwari et al., 2000).

Pain perception among racial and ethnic disparities are differently perceived and tolerated. The inter-individual differences in pain sensitivity are reported to be heritable as the result of polymorphisms of pain-relevant genes (Kim et al., 2004; Uhl et al., 1999). Nepalese and Indian found to have more tolerated to pain compared to Caucasian and Hispanic (Carmen et al., 2003). The different pain perception might be related to the interaction between endorphin and the important primary targeting receptor that is, μ-receptor (Ikeda et al, 2005). The μ-receptor1 is known to be polymorphic especially at the locus of A118G (Lotsch et al., 2005). The variants of A118G might confer the different effect of pain perception which will be under-interpreted in A118G variants group as atypical myocardial infarction. For those who presented with chest pain, the nature of the pain was described as pricking and burning. Kontos and colleagues also identified that burning sensation as in classic chest pain may be suggestive of myocardial ischaemia (Bardy, 1997; Kantos and Jesse, 1997; Selke et al., 1995). Beside the aforementioned presentations, cough, giddiness and epigastric pain were significantly present in the atypical ACS presentation. These non specific associated symptoms may be related to the neuronal stimulation in response to ischaemia and may be also related to the non-independent underlying medical illness such as diabetes mellitus and hypertension or stress related mechanism (Terkelsen et al., 2005).

In our study, 41% (106) patients suffered from DM. Of this number, 27% of diabetic patients who had coronary artery disease presented with atypical chest pain as
compared to atypical chest pain (13.8%). There was a significant difference in clinical presentation between typical and atypical presentation of ACS among diabetic patients. Our findings again re-emphasize the importance of DM as an important independent predictor of a probability of ACS or CAD in our population. High blood sugar and duration of diabetes in uncontrolled diabetes will damage the nerve cells (Angelika et al., 2004). Subsequently, peripheral neuropathy, autonomic neuropathy and focal neuropathy may affect the pain perception (AOL Health, 2007). Loss of autonomic function will affect the nerve conduction to the heart subsequently affect the sweating mechanism, pain perception and the heart rate control that occurs unpredictably. Hence, patients with diabetic might perceive pain differently as atypical in nature.

Interestingly, past history of IHD was associated with typical presentation of myocardial infarction. The possible explanation is the brain learns from its past experience. Well established medical history and experienced of having previous angina pain may alert the patients regarding their illness and make them aware about the consequence of acute coronary disease (Arntz and Claassens, 2004; Katja et al., 2008). Consequence, any chest discomfort or abnormal feelings directly will make them concern about risk of having a new episode of acute myocardial infarction.

In conclusion, atypical presentation of ACS is common and consisted of a quarter of our local population. A greater awareness of atypical presentation may improve awareness among medical personals working in emergency care setting. High index of suspicion with very skilful history clerking and examination may reduce the missed diagnose of acute myocardial infarction.

REFERENCES


Collagen deposition and cellular viability among UVB irradiated human dermal fibroblasts treated by platelets

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Prolonged or repeated low energy ultraviolet B (UVB) irradiation that can inhibit fibroblast proliferation, collagen synthesis, and stimulate collagen degradation is basic concept of skin photo-aging. Recently, a study showed that human skin fibroblasts treated with platelets resulted in a significant higher proliferation rates compared to placebo. The effect of platelets in photo aged human skin fibroblasts, however, is still unclear. To know the effect of platelets to UVB irradiated fibroblasts focusing on proliferation rate and extracellular collagen deposition, various platelet concentrations were given to UVB irradiated normal human dermal fibroblasts. Fibroblast viability rates were determined by MTT-assay, whereas collagen deposition levels were determined by insoluble collagen Sirius red-assay. Data were analyzed by Kruskal-Wallis H and post-hoc by Mann-Whitney U. \( p < 0.05 \) is accepted for significance difference. A group treated by 1.25 normal platelet concentration showed an increase cellular viability rates and collagen deposition level significantly \( (p<0.01) \). As a conclusion, platelet in 1.25 normal platelet concentrations may be a promising modality for the treatment of photo-aging skin.

Key words: Platelet, ultraviolet B (UVB), fibroblast proliferation, collagen deposition.

INTRODUCTION

Sunlight radiation, especially prolonged low energy ultraviolet B radiation, is able to inhibit normal skin fibroblast proliferation (Yamauchi et al., 1988; Chung et al., 2001) and stimulate matrix metalloproteinase expression to digest collagen fibers (Menter et al., 2003; Brennan et al., 2003; Choi et al., 2007) resulting in inhibition further newly collagen synthesis (Varani et al., 2006). Decreasing normal fibroblast proliferation and collagen damage have been accepted as basic concept of UVB induced premature skin aging.

Ultraviolet B induced premature skin aging in molecular level is related with generation of a various reactive oxygen species released by excited skin chromophores (Brenneisen et al., 2002; Dong et al., 2008). Clinicians try to use antioxidants such as vitamin C, selenium, vitamin E and alpha lipoic acid for combating skin aging even though their results show varying degree of success (Stern, 2004). Recently, clinicians tried to use a new modality by using a special technique, namely skin needling, a clinical procedure to perform thousand micropunctures on photo-aged skin to stimulate micro-bleedings. Those bleedings are considered as source of activated platelets. These kind of cell releases enough amount of growth factors which are able to stimulate fibroblast proliferation and collagen synthesis (Fernandes and Signorini, 2008). This technique is based on fact that platelet extravasation during vascular damages not only have important roles in blood clotting but they also produce various cytokines which are able to stimulate cell proliferation as well as collagen synthesis as shown in periodontal regeneration (Nevins et al., 2003) and cell migration (Ray et al., 2003), and human skin fibroblast proliferation (Kakudo et al., 2008; Krasna et al., 2007).

Here, we reported the effect of platelets in UVBirradiated human dermal fibroblast viability rates and extracellular collagen deposition.

MATERIALS AND METHODS

Preparation of the cell culture

Human fibroblasts from foreskin of healthy boys were cultured using...
the explant technique as described previously (Viale, 2000). The cells were cultured in Dulbecco modified Eagle medium with 4.5 g/L D-glucose, 2 mmol/L L-glutamine, 2.5 mg/L amphotericin B, 100 ug/L streptomycin, 100 unit/L penicillin, and 10% bovine serum. All material was purchased from Gibco-USA. The forth passage was used for the experiment.

Preparation of platelets

The platelet rich plasma was produced based on Krasna et al. (2007) method. Twenty milliliters of whole blood with known platelet concentration was centrifuged for 7 min at 280 g at room temperature. The plasma was decanted up to the erythrocyte sediment and then centrifuged again for 7 min at 1290 g at room temperature. Finally, the plasma was decanted and the sediment was re-suspended with 1000 μl plasma. The platelet concentration in this PRP was counted manually in the Neubauer chamber. The PRP was then diluted with plasma corresponding to 0.325 normal platelet concentrations (NPC), 0.625 NPC, and 1.25 NPC.

Experiment

Experiment was designed to compare fibroblast proliferation and collagen deposition among control, UVB+placebo, UVB+0.3125 NPC, UVB+0.625 NPC, and UVB+1.25 NPC groups.

Cells coating and UVB irradiation

Two plates (one for collagen assay and another for MTT assay) of 96 wells were filled with 200 μl of 2 x 10^5 fibroblasts suspension in column 1st, 7th, 8th, 9th, 10th, and 11th. Column 2nd to 6th were remain empty and they were used as a separation distance between irradiated and non irradiated group by covered column 1st to 6th with black-plastic band on the top of plate covers. After 72 hours of incubation to allow collagen synthesis, the medium were then aspirated and replaced with same volume of PBS and a 100 μJ/cm^2 of UVB then were given. The PBS was replaced with fresh medium and all of plates were then re-incubated for 72 h.

PRP treatments

All of medium was aspirated. UVB treated fibroblasts in 7th, 8th, 9th columns were treated with PRP of 0.325 NPC, 0.625 NPC and 1.25 NPC respectively for 72 h. UVB treated fibroblasts in column 10th were filled with plasma as placebo and that in column 11th was left untreated as control.

Fibroblast viability assay

All of plasma was aspirated and the wells were rinsed using PBS for 3 times, 10 min each. Two hundred μl of fresh medium were filled into each well and 50 μl 50 mg/ml MTT (MP Biomedicals-USA) were added. The plate was covered by alluminium foil and incubated for 6 h in 37°C. Medium containing MTT was aspirated and 200 μl DMSO was then filled into each well followed by 25 μl glycine buffer on the top. Optical density was immediately read by 570 nm filtered spectrometer.

Collagen deposition assay

This assay was based on insoluble collagen Sirius Red(Taskiran et al., 1999). Briefly, after washing the wells with PBS, cells were fixed with Bovin solution for an hour, and were then rinsed with tap water until yellow color was completely removed. The plates were let to dry in room temperature for overnight. Two hundred μl of Sirius Red (Sigma-Aldrich, USA) was diluted in saturated picric acid and was subsequently added for each well for an hour. Unbinding Sirius Red was removed by washing four times with 200 μl 0.1 N HCl until supernantant looked clear. The binding Sirius Red was diluted in 200 μl 0.5 N NaOH and their optical density were read by 550 nm filtered spectrometer.

Statistical analysis

Data were analyzed by Kruskal-Wallis H and post-hoc by Mann-Whitney U. p <0.05 is accepted for significance difference.

RESULTS

From Figure 1, it can be seen that 100 mJ/cm^2 of UVB inhibited fibroblast viability rates and this suppression effect was restored by treatment of platelets of 1.25 NPC. Similarly with effect of platelets on fibroblast viability, 100 mJ/cm^2 of UVB irradiation also suppressed collagen deposition and treatment with platelets of 0.3125 NPC and 0.625 NPC revealed various lesser collagen deposition and treatment with platelets in 1.250 NPC showed a reappe the suppression effect (Figure 2).

DISCUSSION

Repeated irradiations with low dosage of UVB light is accepted as an important factor in solar induced photo-aged skin as proven in various experiments. Experiment on hairless mice showed that repeated radiation of low energy of UVB were able to stimulate synthesis of elastin fibers around hair follicles (Starcher et al., 1999) and permanent skin wrinkles even though irradiation had been terminated (Kambayashi et al., 2001), and decrease collagen synthesis (Takema et al., 1996). Those findings are also supported by finding on human skin organotypic experiments (Paquet et al., 1996) and observation of pro-collagen expression among exposed human skin in mRNA level (Chung et al., 2001) as well as in protein level. The central roles of UVB in UVB induced skin wrinkles are based in the ability of UVB to induce DNA damages, either by direct or indirect effect through free radical formation. DNA damages may inhibit cell proliferation due to lengthening of G1 arrest, stimulate collagen degradation due to activation of matrix metalloproteinase, and inhibit collagen synthesis and deposition through methylation of collagen promotor region (Ellis et al., 1988; Myllyharju and Kivirikko, 2004). In addition, degraded collagen materials are also able to inhibit newly collagen synthesis caused by reducing dermal mechanical tensions (Varani et al., 2006).

Human’s periphery blood isolated platelets is proven capable to stimulate fibroblast proliferation (Kakudo et al., 2008; Krasna et al., 2007; Liu et al., 2002), even frozen
Figure 1. The Effect of platelets on fibroblast viability.

Figure 2. The effect of platelets on collagen deposition.
platelets are still able to stimulate healing of chronic ulcers (Crovetti et al., 2004; Pietramaggiore et al., 2010).

It is due to their PDGF secretion that stimulates resting fibroblasts become migrated and proliferated cells (Ray et al., 2003; Li et al., 2004) through mechanism of PCNA activation and synthesis TGF-β (Pan et al., 2007) based on JAK-STAT signaling pathways (Vij et al., 2008).

Several limitations of this study were source of fibroblasts which originated from young human skin and the UVB irradiation which was performed in a single exposure. The ideal study should be performed among old skin human fibroblasts and UVB irradiation should be in repeated low dosage procedures. Since this study aimed to explore the fibroblast viability and collagen deposition rates where these variables could be measured from either old or young skin fibroblasts, therefore young skin fibroblasts were chosen due to practical consideration. A study to measure effect of UVB on human young skin fibroblasts producing collagen, MMPs and TGF-β1 expression under single UVB exposure has been reported before (Choi et al., 2007).

Single exposure UVB was also used to explore basic mechanism of alteration of collagen homeostasis induced by UVB (Quan et al., 2010).

From Figure 1, it can be observed that the minimal dose of platelets capable to restore viability of UVB irradiated fibroblasts was 1.25 normal platelet concentration. Lesser dose of platelets was not able to restore UVB irradiated fibroblast proliferation rates. Platelets will release growth factors after binding with type-I collagen (Fufa et al., 2008) or fibronectin (Nievelstein et al., 1988) and they will release PDGF stimulating TGF-β secretion either by platelets or by PDGF activated fibroblasts (Vij et al., 2008). Exogenous TGF-β has been proven capable to stimulate fibroblast proliferation as well as newly collagen synthesis (Younai et al., 1994; Hsu and Chang, 2004) and deposit them onto extracellular matrix.

Evaluating effect of platelets on collagen deposition, it was shown that 0.325 NPC as well as 0.625 NPC gave various lesser collagen deposition than UVB treated group significantly (P<0.05). A previous study showed that platelets were able to release various MMPs (Kazes et al., 2000).

Those MMPs might able to stimulate additional collagen degradation, thus they reduced collagen deposition. In this figure, it was also shown that addition of platelets in 1.25 NPC was able to stimulate collagen deposition significantly (P<0.05). Number of collagen deposited in this group was higher compared to that of UVB irradiated group and control. We assume that effect of growth factors of 1.25 NPC was superior than that of their released MMPs. These results were consistent with fibroblast proliferation parameter.

Recent studies showed that activated platelets might release various growth factors and their concentrations were higher on PRP technique compared to the plasma levels (Eppley et al., 2004; Frechette et al., 2005).

Incubation platelet gel in 4°C for an hour has been considered as an easy technique to isolate growth factors released by platelets (Anitua et al., 2009). These findings lead clinicians to design a clinical experiment to choose either skin needling, injection of platelets, application of platelet gel, injection of growth factor produced by platelets, or topical application of growth factors produced by platelets as the best way to treat photo-aged skins.

Conclusions

Activated platelet in the concentration of at least 1.25 normal platelet concentrations showed both restoration of UVB-inhibited fibroblast viability and UVB-suppressed collagen deposition. Platelets might be used as treatment of UVB induced skin aging. Further research should be performed to verify and expand this results.

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**2013**

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