

EFEK PEMBERIAN KALSITRIOL ($1\alpha,25$ (OH) $_2$ D $_3$) TERHADAP KEMAMPUAN KONTRAKSI KULTUR KARDIOMIOSIT Kajian terhadap fosforilasi troponin I dan kadar cyclic AMP

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INTISARI

Latar belakang: Defisiensi vitamin D meningkatkan faktor risiko terjadinya penyakit kardiovaskular. Kalsitriol (bentuk aktif vitamin D) melalui fosforilasi troponin I berperan dalam regulasi respon frekuensi dan kekuatan pada proses ejeksi ventrikel. Jalur mekanisme fosforilasi troponin I (TnI) salah satunya melalui cAMP/PKA. Penelitian ini bertujuan untuk mempelajari efek kalsitriol terhadap peningkatan fosforilasi TnI serta jalur mekanisme aksinya yang melalui cAMP/PKA.

Metode: Penelitian ini merupakan penelitian eksperimental murni menggunakan rancangan *pre-post test with control group* dengan sampel kultur primer kardiomiosit Sprague-Dawley jantan dewasa yang dibagi dalam 6 kelompok. Kardiomiosit diinkubasi kalsitriol selama 5 menit kemudian fosforilasi TnI dinilai dengan teknik *immunocytochemistry* (ICC) menggunakan antibodi phospho-Ser22+Ser23 dan jumlah sel dengan TnI yang terfosforilasi dihitung menggunakan *software image raster*. Kadar cAMP diukur menggunakan metode ELISA.

Hasil Penelitian: Perbedaan TnI yang terfosforilasi pre dan post test yang bermakna ($p < 0,05$) dijumpai pada setiap kelompok dengan nilai rerata \pm SD (intensitas kuat, sedang dan lemah secara berurutan) sebagai berikut: pretest: (7,83 \pm 4,08)%; (26,27 \pm 3,00)%; (65,89 \pm 2,46)%, K(-): (2,89 \pm 2,65)%; (25,9 \pm 8,48)%; (71,22 \pm 10,67)%, D1: (21,57 \pm 13,86)%; (54,75 \pm 19,09)%; (23,69 \pm 9,39)%, D2: (23,42 \pm 10,33)%; (72,45 \pm 10,49)%; (4,14 \pm 3,35)%, D3: (29,92 \pm 9,51)%; (61,09 \pm 7,35)%; (8,99 \pm 4,13)%, K(+): (57,05 \pm 23,01)%; (34,95 \pm 16,78)%; (8,01 \pm 7,95)%. Kadar cAMP pre dan post test setiap kelompok tidak mengalami peningkatan, dengan nilai rerata \pm SD sebagai berikut: pretest (307,67 \pm 47,78 pmol/mL); K(-) (285,92 \pm 46,63 pmol/mL); D1 (282,86 \pm 19,41 pmol/mL); D2 (209,39 \pm 33,58 pmol/mL), D3 (188,93 \pm 34,16 pmol/mL) dan K(+) (175,20 \pm 6,64 pmol/mL). Tidak dijumpai korelasi yang bermakna antara peningkatan TnI yang terfosforilasi dengan penurunan kadar cAMP ($p > 0,05$).

Kesimpulan: Inkubasi kalsitriol selama 5 menit dapat meningkatkan fosforilasi TnI, akan tetapi jalur aktivasi cAMP/PKA oleh kalsitriol belum terbukti.

Kata kunci: Kalsitriol, kontraktilitas, kardiomiosit, cAMP, Troponin I.

CALCITRIOL ($1\alpha,25$ (OH) $_2$ D $_3$) EFFECTS ON CULTURED CARDIOMYOCYTES CONTRACTILE ABILITY

A study on phosphorylated-troponin I and cyclic AMP level of cardiomyocytes

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ABSTRACT

Background: Vitamin D deficiency is associated with increasing risk of cardiovascular diseases. Calcitriol (active form of vitamin D), through phosphorylated-cardiac troponin I (cTnI), contributes in regulation of ventricular ejection force and frequency response. One of calcitriol action mechanism in troponin I phosphorylation process is through cAMP/PKA pathway. The aim of this research is to know the calcitriol effect on increasing cardiomyocytes phosphorylated-troponin I and the involvement of cAMP/PKA signaling cascade.

Methods: This is a true experimental pre-post test with control group design study. It used primary cultured cardiomyocytes of adult male Sprague-Dawley ventricles which was divided in 6 groups, as the samples. Cardiomyocytes was incubated in calcitriol for 5 minutes, then phosphorylated-troponin I was assessed with immunocytochemistry technique using phospho-Ser22+Ser23 antibody and then counted by image raster software. Cardiomyocytes cAMP level was measured by ELISA method.

Results: Significant difference of pre-post test phosphorylated-troponin I was observed in each groups ($p < 0,05$). Mean \pm SD of cardiomyocytes phosphorylated-troponin I as high, intermediate and low intensity for each groups consecutively shows below: pretest: (7,83 \pm 4,08)%; (26,27 \pm 3,00)%; (65,89 \pm 2,46)%, K(-): (2,89 \pm 2,65)%; (25,9 \pm 8,48)%; (71,22 \pm 10,67)%, D1: (21,57 \pm 13,86)%; (54,75 \pm 19,09)%; (23,69 \pm 9,39)%, D2: (23,42 \pm 10,33)%; (72,45 \pm 10,49)%; (4,14 \pm 3,35)%, D3: (29,92 \pm 9,51)%; (61,09 \pm 7,35)%; (8,99 \pm 4,13)%, K(+): (57,05 \pm 23,01)%; (34,95 \pm 16,78)%; (8,01 \pm 7,95)%. There was no increased of cAMP level in each groups, with mean \pm SD of each groups as shown below: pretest (307,67 \pm 47,78 pmol/mL); K(-) (285,92 \pm 46,63 pmol/mL); D1 (282,86 \pm 19,41 pmol/mL); D2 (209,39 \pm 33,58 pmol/mL), D3 (188,93 \pm 34,16 pmol/mL) dan K(+) (175,20 \pm 6,64 pmol/mL). There was also no significant correlation observed between increased phosphorylated-troponin I and decreased cAMP level in this research ($p > 0,05$).

Conclusion: Incubating in calcitriol for 5 minutes elevated cardiomyocytes phosphorylated-troponin I, nevertheless the involvement of cAMP/PKA signaling cascade in this action was still uncertain.

Keywords: Calcitriol, contractility, cardiomyocytes, cAMP, phosphorylated-troponin I.