

PAIN IN CHILDREN WITH LEUKEMIA

Cempaka Thursina Srie Setyaningrum¹, Kusumo Dananjoyo¹, Ismail Setyopranoto¹, Sri Sutarni¹, Indarwati Setyaningsih¹, Agus Budi Bowo Leksono¹, Rosmala Nur², Muh Zainuddin Badollahi³

¹Departemen Neurologi FK-KMK UGM / RSUP Dr. Sardjito Yogyakarta

²Departemen of Public Health, Faculty of Public Health-Universitas Tadulako, Palu, Indonesia

³Program Studi Antropologi, Universitas Tadulako, Indonesia

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Corresponding Author:

Cempaka Thursina Srie Setyaningrum

Email:

cempakasetyaningrum@gmail.com

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ABSTRACT

Painful is Wrong One factor main in management patient with cancer. Pain Also is common problems neglected on malignancy blood, where painful cancer blood is often late recognized And Wrong treated. Sufferer can report existence a number of site painful different anatomy , which may due to by cancer , by maintenance cancer , by weakness general or by disturbance simultaneously. Painful on cancer Also must associated with a number of symptom physique other And with all symptom psychological assessed, including difficult sleep, worry, trouble concentrate, and feel sad , nervous , or easy angry . The pain on children with leukemia originates from four source. First that is pain caused by source his illness alone , 25% of the pain that appears more beginning is painful bones , because infiltration by bone or joints because of proliferation immature cell blood white .), second , Procedure For diagnosis and enforcement therapy invasive disease And painful , third , effect side procedure And chemotherapy that causes effect pain , fourth , child with leukemia who feel pain that is not relate with the disease suffered Evaluation separated from each syndrome painful must For management optimal leukemia pain . Pain must be evaluated in a way regular as 5th vital sign. Intensity pain can recorded by a number of tools, such as verbal description, visual analog scale (VAS) and numeric rating scale (NRS). Tools This Possible No in accordance For a number of patients, such as child, patient mature No communicative And No aware , where expression face and verbal and non-verbal descriptors can used. You are neat on Chemotherapy patients induction can considered as action etiological Because its powerful effect No only in relieve pain , especially painful bone fierce , but Also in relieve pain Because default disease , which responds dramatically in most case . Therapy pharmacological can involving opioids, NSAIDs, acetaminophen , and adjuvant in accordance with etiology type leukemia And complications involved.

INTRODUCTION

Cancer is Wrong One reason main death of 90,000 children every year. In the country earn high, cancer is reason second the biggest death child aged 5-14 years after injury and accident. Around 3,000 children diagnosed with acute leukemia in the United States every year, with incidence 4.2:100,000 in children skin white and 2.4:100,000 on children black skin ¹.

Of the total number of children suffering cancer, more from 80% of all over children This will experiencing pain on a number of point in journey cancer they are good as consequence from disease they myself, as effect side from its maintenance, or as consequence from related

procedures with their care². Almost one in three leukemia patients, especially child, have incidence leptomeningeal, cranial, and intracranial infiltration radix spinal nerves. Incidence more heavy in acute leukemia compared to chronicle And more big on leukemia type lymphocytic compared to myelocytic³.

Regardless from type from leukemia, the emergence of symptom beginning from each type leukemia Good from aspect his illness, and the procedure undergone, pain will become almost complaint always diala mi by child with leukemia⁴. Top base the so need made a review purpose-built library For compiled related articles with characteristics painful from child with leukemia, as well as his needs in integration from Handling painful And palliative oncology pediatric during treatment.

LEUKEMIA

Leukemia is a disease malignancy cell blood white that comes from from marrow bones , caused by a number of factor risk during pregnancy And post christmas like disability genetics , radiation , infection And exposure others , marked by existence accumulation proliferation leukocytes And abnormal cells in marrow bone And blood , can cause complications in the form of sepsis, disorders freezing blood or consequence chemotherapy , has a prognosis that is difficult to determine^{5,6}.

In general, leukemia is divided into acute, chronic and congenital. Acute and chronic leukemia were initially distinguished based on the duration of the disease during effective chemotherapy, but currently acute and chronic are distinguished based on the type of cell where malignant immature cells that proliferate lead to acute leukemia and if there are more mature cells then it is classified as chronic leukemia, while congenital when leukemia is diagnosed during the first 4 weeks after birth⁷.

PAIN IN LEUKEMIA

Painful on children with leukemia originate from four source. First that is pain caused by source his illness alone, 25% of the pain that appears more beginning is painful bones, because infiltration by bone or joints because of proliferation immature cell white blood¹. Second, Procedure For diagnosis and enforcement therapy invasive disease And painful, like *Multiple venipunctures*, aspiration marrow bone , function lumbar , catheterization central . Third, the effect side procedure And chemotherapy that causes effect pain, such as painful on lesi aspiration marrow bone, pain head after done lumbar function, and painful muscle after enter chemotherapy . Fourth, children with leukemia that feel pain that is not relate with disease suffered⁴.

Connection between the pain And time from the onset of chemotherapy show that , different with other malignancies , pain on patient with results Leukemia I especially from maintenance And complications . All symptom physique relate with great pain in our research is almost always accompanied by existence complications lack of energy , hair fall out , sweat , mouth sores , swelling , numbness / tingling in hands or feet, and difficulty swallowing⁸.

Table 1. Syndromes painful on cancer blood

Type Painful	Subtype Painful	Etiology And pathogenesis
Nociceptive	Somatic In	Related Disease : Bone : Infiltration marrow bone (leukemia acute), Lesions osteolytic (Myeloma), disease other bones (inflammation , microfractures) Involvement extramedullary : CNS: pain head , enlargement spleen And liver (distension capsular)
		Complications Disease :

		Infection (abscess , cellulitis , pleurisy) , deep vein thrombosis , spasm muscle And contracture , atrophy muscle	
		Procedure diagnostic And maintenance : Painful procedural (biopsy) marrow bone , pain lumbar post head puncture , catheterization) , mobilization , transport patient .	
		Related therapy : Expansion marrow bone Because hormone growth , osteoporosis and myopathy steroid- related , deep vein thrombosis related therapy .	
	Superficial somatic	Related disease : Ulceration skin due to malignancy	
		Complications disease : Ulceration cutaneous , oral, and conjunctiva caused by viral, fungal and bacteria , ulcer peptic ulcer , <i>Graft versus host disease</i> (GVHD) ocular	
		Iatrogenic : Oral mucositis , venipuncture , insertion central venous catheter , biopsy skin , cutaneous GVHD	
	Visceral	Related disease : Compression visceral Because enlargement lymphophonediode And organomegaly (spleen) or heart)	
		Complications disease : Infection visceral <i>varicella zoster</i> (seldom).	
		Iatrogenic : Pancreatitis L- asparaginase induction , constipation And megacolon induction <i>thalidomide</i> or <i>vincristine</i> , Induced intestinal neuropathy bortezomib , gastrointestinal mucosa , typhlitis , appendicitis , intestinal pneumatosis , perianal infection , irritation womb urine And cystitis , gastrointestinal GVHD .	
	Neuropathic	Periphery	Related disease : Irritation nerve peripheral marrow bone , clamping nerve And root nerves , neuropathy peripheral (amyloid, paraprotein) , plexopathy Because infiltration tumor
			Complications disease : Infection <i>herpes zoster</i> , postherpetic neuralgia , neuropathy or radiculopathy autoimmune and also infectious .
			Iatrogenic : Neuropathic periphery induction drugs (bortezomib , thalidomide)
Central		Spinal cord compression , stroke, tumor brain	
Functional		Sensitivity painful without deficit neurological or peripheral	
Mixture	Neuropathic + somatic	Complications disease : Combination from all that is called on	
Breakthrough	Incident : related movement realized and also No realized	Complications related drug : Visceral (spasm , tenemus) and somatic (allodynia , spasms) muscle , mobilization)	
		Iatrogenic : Mastication And swallowing (oral mucositis)	
	Non incident	Failure dose end , neuropathy peripheral Because other reasons	

Painful iatrogenic And related maintenance almost always relate with procedure diagnostic like lumbar bone marrow puncture , biopsy / aspiration ⁹. Related with maintenance often happen on venipuncture , insertion catheter , medication , mobilization and also transportation patients . Patients who receive Granulocyte Colony-Stimulating Factor (G-CSFs) therapy for neutropenia is often experience painful bone And headache ¹⁰ . On patients who receive bisphosphate related the violence that attacks bone often happen necrosis bone on jaw that becomes source pain . Mucositis mouth caused chemotherapy using *Hematopoietic Stem Cell Transplantation* (HSCT). Complaint mucositis channel most frequent digestion happen in form painful visceral , which is caused by Graft Versus Host Disease (GVHD). specific induce damage mucosa . Therapy specific such as L- asparaginase And bortezomib can induces pancreatitis ¹¹ , neuropathy interstitial And intestinal dysmotility ⁹ . Thalidomide and vincristine therapy can induce constipation that becomes reason visceral pain ¹² .

LEUKEMIA PAIN MANAGEMENT

Chemotherapy induction can considered as " action etiological " because its powerful effect No only in relieve pain, especially painful bone fierce , but Also in relieve pain Because default disease , which responds dramatically in most cases . As well as corticosteroids Can considered as targeted treatment For part big leukemia , especially For lymphoid . In addition relieve pain bone , corticosteroids very effective when it hurts relate with infiltration nerve or compression structure nerves , as observed on patient with compression marrow bone behind , where dexamethasone dose tall can cause sudden pain relief ; even , corticosteroids together with mannitol can own role important on patient with meningopathy and / or involvement disease brain with reduce pressure intracranial as well as effect compression to adjacent structures with enlargement gland sap clear can removed with this agent ⁹ .

Radiotherapy effective For control pain consequence lesi bone And compression marrow spine ⁹ . Some regimen different radiotherapy in timetable fractionation , usually used in practice clinical , appropriate with objective clinical And base radiobiological leading to subtraction painful and the calcification process repeat . special For effect analgesic , dosage low 8 Gy fraction single recommended For palliative painful on lesi bone local , especially in performance status case low patient And hope short life . Multi - fraction schedule given in longer time for example (40-44 Gy /20-22 fractions /4 weeks , or 30 Gy /10 fractions / 2 weeks) is given For patient with age hope long life And give choice painkiller best And Also recovery bone structure ¹⁰ . For patient with lesi osteolytic big on the bones that hold load , tool orthopedics And procedure operation can reach control painful And prevention fracture that will come . In a number of year Lastly , percutaneous cementoplasty , vertebroplasty And kyphoplasty has developed For repair fracture bone behind and to give painkiller on patient with multiple myeloma (MM) ¹³ .

PHARMACOLOGICAL THERAPY FOR LEUKEMIA PAIN

Principle therapy painful state oral route is more recommended on part big patient , but ways other administration (rectal , subcutaneous, sublingual) And etc.) can considered . Route intravenous is method fastest For reach analgesic effect on patient with increasing pain fast or uncontrolled ¹⁴ .

Dose is part important on governance children . Some big drug on children given dose in accordance with heavy body (mg/kg) or wide surface body (mg/m²). Treatment must taken For Correct convert heavy body from pounds to kilograms (1kg = 2.2lb) before count dose based on heavy body . Dosage often stated as mg/kg/ day or mg/kg/ dose , Drugs chemotherapy usually given dose in accordance with wide surface body , which requires step verification additional (calculation) wide body) before giving dosage . Drug available in various concentration , by Because That written order in "mL" rather than "mg" no can accepted And need clarification more

Continue . Dosage Also varies based on indication , by Because That information diagnostic very help when calculate dose ¹⁵ .

OPIOID

Opioid administration depends from intensity pain (moderate) and also weight) recommended , opioids are classified as a weak opioid And strong . Therapy use morphine need deep knowledge around potential each medicine , especially is morphine which has been This considered as “ therapy” main ” effect analgesic from all opioids. Bioavailability around each opioid and route administration as well as titration is a must ¹⁶ . Dosage morphine on child is 0.15-0.3 mg/ kgBW every 4 hours orally and 50-100µg/ kgBW every 2-4 hours for intravenous administration ¹⁷ .

NON-OPIOID

Analgesic standard , such as paracetamol , dosage paracetamol For children is 10-15 mg per kilogram of weight . medicine anti-inflammatory nonsteroidal (NSAID), can used For painful nociceptive . Management painful light up to what is experienced by patient with leukemia , paracetamol play role Key . Agent This No inhibits peripheral prostaglandins , and Because That No deploy influence whatever on system coagulative ; so that show more profile safe than NSAIDs, although its use need attention existence liver disorders ¹⁸ .

NSAIDs are very effective in relieve painful bones , especially on patient with Leukemia ; However , the occurrence of dysfunction kidney And existence improvement risk bleeding Because thrombocytopenia often found in use agent This so that requires caution ¹⁴ .

CONCLUSION

Pain that originates from etiology leukemia divided becomes painful nociceptive, neuropathic, visceral, and functional. Degree pain that is obtained must checked and evaluated routine use tool the size that has been standardized like visual analog scale (VAS) and numeric rating scale (NRS), Use tool support Good radiological and also electrophysiological must returned to needs clinical each patient. On distribution type leukemia, prevalence painful taller on leukemia I compared to chronic.

Management painful on patient child with leukemia must be done since patient has diagnosed, prevention pain is objective main from all over management pain. Administration therapy oral route is route main when allow However nature flexible, returnable to condition clinical patient each.

REFERENCES

1. Crist, W.M., & Pui, C. (1996). Neoplastic diseases and tumors: Leukemias. In R.E. Behrman, R.M. Kliegman, & A.M. Arvin (Eds.), *Nelson Textbook of Pediatrics* (15th ed.) (pp. 1452-1455). Philadelphia: W.B. Saunders.
2. Duffy, E. A., Dias, N., Hendricks-ferguson, V., Hellsten, M., Skeens-borland, M., Thornton, C., & Linder, L. A. (2019). Seminars in Oncology Nursing Perspectives on Cancer Pain Assessment and Management in Children, 35. <https://doi.org/10.1016/j.soncn.2019.04.007>
3. Ropper, A.H., Samuels, M.A. Klein, J.P. & Prasad, S. 2019. *Adams and Victor's Principles of Neurology 11th Edition*. 11th ed. A. H. Ropper, M.A. Samuels, J.P. Klein, & S. Prasad, eds. New York: McGraw-Hill
4. Bossert, E. A., Cleve, L. Van, Adlard, K., & Savedra, M. (2002). Pain and Leukemia : The Stories of Three Children, 19(1), 2–11. <https://doi.org/10.1053/jpon.2002.30011>
5. Parmono B, Sutaryo, Ugrasena IDG, Windiastuti E, Abdulsalam M, Leukemia Akut; Kedaruratan Onkologi Anak dalam Buku Ajar Hematologi – Onkologi Anak 2010 : 236 – 325

6. Crist, W.M., & Pui, C. (1996). Neoplastic diseases and tumors: Leukemias. In R.E. Behrman, R.M. Kliegman, & A.M. Arvin (Eds.), *Nelson Textbook of Pediatrics* (15th ed.) (pp. 1452-1455). Philadelphia: W.B. Saunders.
7. Green T, Franklin W, Tanz RR,. 2005. Leukemia in Pediatrics Just the Facts : 376 – 377
8. Shaulov, A., Rodin, G., Popovic, G., Caraiscos, V. B., Le, L. W., Rydall, A., Zimmermann, C. (2018). Pain in patients with newly diagnosed or relapsed acute leukemia.
9. Niscola P, Scaramucci L, Romani C, Giovannini M, Tendas A, Brunetti G, et al., 2010. Pain management in multiple myeloma. *Expert Rev Anticancer Ther*;10:415–25.
10. Pinto L, Liu Z, Doan Q, Bernal M, Dubois R, Lyman G, 2007. Comparison of pegfilgrastim with filgrastim on febrile neutropenia, grade IV neutropenia and bone pain: A meta-analysis of randomized controlled trials. *Curr Med Res Opin*;23:2283–95.
11. Flores-Calderón J, Exiga-González E, Morán-Villota S, Martín-Trejo J, Yamamoto-Nagano A,. 2009. Acute pancreatitis in children with acute lymphoblastic leukemia treated with L-asparaginase. *J Pediatr Hematol Oncol*.31:790–3.
12. Diezi M, Nydegger A, Di Paolo ER, Kuchler H, Beck-Popovic M,. 2010. Vincristine and intestinal pseudo-obstruction in children: Report of 5 cases, literature review, and suggested management. *J Pediatr Hematol Oncol* ;32:e126–30.
13. Garland P, Gishen P, Rahemtulla A,. 2010. Percutaneous vertebroplasty to treat painful myelomatous vertebral deposits long-term efficacy outcomes. *Ann Hematol*;90:95–100.
14. Mercadante S, 2010. Intravenous morphine for management of cancer pain. *Lancet Oncol*;11:484–9.
15. Van-Gijn J., Rinkel G.J.E., 2001. Subarachnoid haemorrhage: diagnosis, causes and management, *Brain Journal*;124:249-278.
16. Tremblay J, Hamet P, authors. Genetics of pain, opioids, and opioid responsiveness. *Metabolism*. 2010;59(Suppl 1):S5–8.
17. Friedrichsdorf Stefan J., Postier A., 2014. Management of breakthrough pain in children with cancer. Minnesota: Dovepress.
18. Smith H, Bruckenthal P,. 2010. Implications of opioid analgesia for medically complicated patients. *Drugs Aging* ;27:417–33.